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# DIAGNOSIS AND TREATMENT OF NUTRITIONAL ANEMIA

*Byron E. Hall, M.D., San Francisco*

The term nutritional anemia signifies an anemia due to inadequate intake or faulty absorption and assimilation from the gastrointestinal tract of hemopoietic factors normally present in food. The list of factors known to be essential for erythropoiesis to proceed normally includes certain amino acids, minerals (iron, copper, cobalt, and possibly others), and vitamins, the members of the B group being the most important, although recent evidence suggests that ascorbic acid plays a vital ancillary role. Important B vitamins include pyridoxine, riboflavin, niacin, folic acid, and vitamin $B_{12}$. Leuconostoc citrovorum factor (probably synonymous with folinic acid), a substance known to be related to folic acid, also has hemopoietic properties. A vast literature has accumulated with regard to the role that each of these substances plays in the formation of erythrocytes, but the relationships of these compounds to one another and to certain metabolic processes as yet are incompletely understood. Several excellent reviews of the literature on the more recently discovered hemopoietic agents have been published.[1]

Nutritional anemia is seen infrequently in the North Central states. The rarity of this type of anemia seems to be a reflection of the adequacy of the food ingested by the populace as a whole. This is in striking contrast to the relative prevalence of nutritional macrocytic anemia and of sprue in tropical and subtropical regions. It is of interest that sprue, a common disease in Puerto Rico only a few years ago, now is reported as being rare, as a result of better nutrition through education and improvement of the economic status of the island's inhabitants.[2]

Anemia due solely to the inadequate intake of essential foodstuffs, while rare in this area, occasionally is encountered in persons suffering from anorexia associated with profound emotional disturbances, adherence to dietary fads, food idiosyncrasies, or poverty. It is seen more frequently in patients with organic disease processes that either interfere with absorption in the alimentary tract of hemopoietic factors present in food or prevent an adequate intake of food. This paper is concerned with two types of nutritional anemia: (1) anemia due to deficiency of iron (hypochromic anemia and iron deficiency anemia), and (2) anemia due to deficiencies of folic acid or of vitamin $B_{12}$ (megaloblastic anemia).

## IRON DEFICIENCY ANEMIA

This form of anemia is characterized by a reduced concentration of hemoglobin in the blood. The number of erythrocytes may be normal or reduced, but in either case the color index is low, the mean corpuscular hemoglobin is reduced, and the mean corpuscular hemoglobin concentration is diminished. The volume of packed erythrocytes may be reduced if microcytosis is present or if the degree of anemia is severe. Stained blood films show hypochromasia of erythrocytes, and examination of the bone marrow shows normoblastic erythropoiesis.

A detailed discussion of factors concerned in the production of this type of anemia is beyond the scope of this paper, but it is pertinent to recall that a state of iron deficiency is seen more frequently among patients suffering from chronic loss of blood than among those in whom the deficiency is the result of an inadequate diet or of faulty absorption associated with disorders of the gastrointestinal tract (regional enteritis, chronic ulcerative colitis, sprue, and extensive resection of the bowel). Moreover, hypochromic anemia tends to develop during periods of rapid growth in infancy, early childhood, or adolescence, and during pregnancy, when the intake of iron may not meet physiological demands.

Utilizing foods tagged with radioiron, Moore and Dubach [3] found that for iron balance to be maintained the normal man must assimilate from 0.5 to 1.0 mg. of iron daily and the normal woman from 1.0 to 2.0 mg. daily, depending on the menstrual loss of blood and the frequency of pregnancies. Ten per cent or less of the iron in the foods fed healthy subjects was absorbed. Administration of ascorbic acid and foods containing ascorbic acid increased the absorption of food iron, but hydrochloric acid and antacids did not. Treatment with inorganic iron in the form of ferrous salts, administered

From Stanford University School of Medicine.
The bibliographic references have been omitted from THE JOURNAL because of lack of space; however, they are included in the author's reprints.
Read before the Joint Meeting of the Section on Gastro-Enterology and Proctology and the Section on Pathology and Physiology at the 101st Annual Session of the American Medical Association, Chicago, June 12, 1952.

orally in adequate dosage, is as specific in producing satisfactory responses in the vast majority of cases as is liver extract or vitamin $B_{12}$ therapy in pernicious anemia. The supplemental use of diets rich in iron and ascorbic acid is advisable, but there is no justification for the administration of liver extract, vitamin $B_{12}$, folic acid, or combinations of these substances with iron to patients having iron deficiency anemia.[4]

Failure of the patient to respond to orally administered iron may be due to (1) intolerance to adequate dosage owing to gastrointestinal irritation, (2) sensitivity to iron,[5] (3) severe gastrointestinal disease in which oral therapy is inadvisable, or (4) refractoriness to oral therapy, presumably the result of an inability to absorb iron from the gastrointestinal tract.[6] In cases such as these, satisfactory clinical and hematological responses may be obtained by intravenous administration of saccharated iron oxide. This compound is relatively nontoxic, and reactions are minimal; however, caution must be used to give only enough iron intravenously to correct the deficiency. Calculation in grams of the total dose of iron required to restore the blood to normal may be made either by multiplying the deficit of hemoglobin (obtained by subtracting the initial value for hemoglobin in grams per 100 cc. from the normal value for hemoglobin in grams per 100 cc.) by the factor 0.255 [5] or by allowing 25 mg. of metallic iron for each 1% deficit in hemoglobin.[4] The total dose then is subdivided into individual daily doses varying from 50 to 150 mg. It is generally not advisable to administer more than 50 mg. as an initial dose. If there is no reaction, 100 to 150 mg. may be given intravenously each day thereafter until the total requirement has been supplied. The effectiveness of intravenous administration of iron is illustrated by case 1.

CASE 1.*—A housewife, 35 years of age, had severe anorexia after a serious injury to an only child. Loss of weight and the development of anemia, cheilosis, and soreness of the mouth followed. Prior to admission, folic acid, vitamin $B_{12}$, and various vitamin preparations, including those of the B group, were given without improvement. Iron was not administered. On admission, the concentration of hemoglobin was 7.6 gm. per 100 cc. of blood and there were 4,690,000 erythrocytes per cubic millimeter of blood. Cheilosis was present, but there was no glossitis. Saccharated iron oxide, 1,350 mg., was administered intravenously over a period of nine days. The concentrations of hemoglobin then had risen to 9.4 gm., and clinical improvement was striking, the latter being manifested by return of appetite to normal, gain in strength, and complete disappearance of the cheilosis. Reexamination of the blood three months later showed 12.8 gm. of hemoglobin per 100 cc. and 4,440,000 erythrocytes.

## MEGALOBLASTIC ANEMIAS

Certain diseases seen in a clinical type of practice drawing patients mainly from North Central states are characterized by megaloblastic erythropoiesis. I will exclude from this discussion the megaloblastic anemias encountered in the tropics (tropical sprue and nutritional macrocytic anemia), nutritional macrocytic anemia of the type seen in certain areas in the southern United States,[7] and the megaloblastic anemia due to infestation with Diphyllobothrium latum observed so frequently in Finland.

*Pernicious Anemia.*—More than 20 years ago, Castle and his associates [8] demonstrated the presence of a substance (gastric or intrinsic factor) in normal human gastric juice, which acted on a dietary substance (food or extrinsic factor) to form a material (antipernicious anemia principle) required for normal maturation of erythrocytes. In the normal person, antipernicious anemia principle was thought to be stored in the liver. In pernicious anemia intrinsic factor was lacking, and hence the product of interaction between extrinsic factor and intrinsic factor could not be formed. Castle, therefore, considered pernicious anemia to be a form of nutritional anemia conditioned by the absence or gross deficiency of intrinsic factor.

After the discovery and isolation of vitamin $B_{12}$, it was found that this member of the B vitamins functioned in the same manner as the antipernicious anemia principle contained in extracts of liver did when vitamin $B_{12}$ was administered parenterally to patients having pernicious anemia in relapse. The vitamin controlled not only the anemia but the neurological manifestations of the disease as well. Shortly thereafter, Berk and his associates [9] showed that vitamin $B_{12}$ also functioned as extrinsic or food factor when administered simultaneously with intrinsic factor to patients having pernicious anemia in relapse. The daily oral administration of 5.0 mg. of the vitamin plus 150 cc. of normal gastric juice elicited optimal or nearly optimal hemopoietic responses. This observation subsequently was confirmed by a number of investigators.[10]

Intrinsic factor, on the other hand, has not been isolated, although many of its properties are known.[11] It is an exceedingly unstable substance that in man is secreted principally by mucosal glands in the fundus of the stomach, in the cardia, and to a lesser extent in the pylorus.[12] In swine, it is present in the pyloric portion of the stomach and in the upper part of the small intestine.[13] It has not been identified with rennin, pepsin, or trypsin.[8] Glass and his associates [14] recently found intrinsic factor activity in gastric mucoprotein obtained from human sources. They concluded that a glandular mucoprotein fraction acts as the main carrier of this activity in human gastric juice. While the potentiating effect of intrinsic factor for effective utilization of small amounts of vitamin $B_{12}$ is well established, the oral administration of large quantities of the vitamin in the absence of intrinsic factor will elicit significant hemopoietic responses in patients having pernicious anemia in relapse.[15]

A suboptimal but significant hemopoietic response to the oral administration of a large quantity of vitamin $B_{12}$† to a patient with pernicious anemia is shown in fig. 1. Vitamin $B_{12}$, 1,000 $\mu$g, was given every second day (the equivalent of 2½ lb. of raw calf's liver daily)[16] for 14 days, and thereafter 1,000 $\mu$g was administered every third day (the equivalent of 1½ lb. of raw calf's liver daily) for 5 months. The response was suboptimal when compared with established standards. A total of 32,000 $\mu$g of vitamin $B_{12}$ was administered in three months before the erythrocyte count rose to more than 4 million per cubic millimeter. Since an optimal response can be obtained in eight weeks by the daily oral administration of 5.0 $\mu$g of vitamin $B_{12}$ and 150 cc. of normal human gastric juice, the total dose of the vitamin required to induce hematological

* Dr. A. B. Hagedorn furnished this case from his series of patients treated with saccharated iron oxide.

† Vitamin $B_{12}$ for this phase of the study was supplied by Merck & Company, Inc., Rahway, N. J.

remission in the presence of intrinsic factor would approximate 280 μg. Thus, the importance of intrinsic factor in potentiating the absorption and utilization from the alimentary tract of the small amounts of vitamin $B_{12}$ normally present in foodstuffs is graphically demonstrated.

That intrinsic factor forms a complex with vitamin $B_{12}$ has been suggested by a number of observations. Ternberg and Eakin [17] demonstrated that vitamin $B_{12}$ was bound by a substance or substances in normal human gastric juice and in the lining of the gastrointestinal tract of certain mammalian species that rendered the vitamin unavailable for the growth of Escherichia coli. Hall and co-workers [10d] also observed that vitamin $B_{12}$ and intrinsic factor united to form a complex possessing greater heat stability than that of intrinsic factor alone. Callender and Lajtha [18] found that in marrow cultures megaloblastic erythropoiesis was unaffected by the addition of vitamin $B_{12}$ alone but the addition of incubated mixtures of vitamin $B_{12}$ and intrinsic factor (normal human gastric juice) promptly resulted in the conversion of megaloblastic to normoblastic erythropoiesis. As a result of these observations, Callender and Lajtha [18] postulated that parenterally administered vitamin $B_{12}$ combines with intrinsic factor obtained from an extragastric source and that the complex formed by the interaction of these two substances is responsible for the hemopoietic activity observed when vitamin $B_{12}$ is administered intramuscularly or intravenously to patients having pernicious anemia in relapse.

The parenteral administration of refined extracts of liver or of vitamin $B_{12}$ continues to be the preferred method of treatment for this disease. Oral therapy is less reliable owing to the difficulty of retaining activity of the intrinsic factor during manufacture of preparations on a commercial basis for oral use. Patients receiving vitamin $B_{12}$ by the oral route, therefore, should be observed closely and parenteral therapy substituted if the hematological and clinical response is unsatisfactory. It would appear to be advisable to reemphasize the fact that folic acid should not be employed in the treatment of pernicious anemia. Although this compound when administered by either the oral or parenteral route will produce hemopoietic responses, the responses so obtained often are suboptimal and in some instances hematological remission is incomplete. Moreover, the neurological manifestations of pernicious anemia may develop or progress among patients treated solely by this method.

*Nontropical Sprue.*—Spies and his associates [19] and others have reported significant hematological and clinical improvement in almost all patients having tropical sprue with megaloblastic anemia who were treated with an adequate diet and with folic acid or vitamin $B_{12}$. Results in nontropical sprue have not been as favorable,[20] even among patients adhering to a complete sprue regimen: a high caloric, high protein, low fat diet; parenteral or oral administration of liver extract, folic acid, or vitamin $B_{12}$; and the supplemental use of soluble calcium and vitamins.

Observations on 17 patients with nontropical sprue, in whom hematological studies of the bone marrow as well as of the peripheral blood were made, may be summarized briefly as follows: Normoblastic erythropoiesis was found in one patient with normocytic normochromic anemia and in two with normocytic hypochromic anemia. Macrocytosis of erythrocytes was observed in 14; of these, normoblastic erythropoiesis was found in 10 and megaloblastic erythropoiesis in 4. The well-known fact that megaloblastosis is by no means a constant finding in this disease, even in the presence of severe or moderately severe degrees of anemia, thus is substantiated. Moreover, response to treatment, although admittedly difficult to analyze, could not be correlated with the type of anemia or with the type of erythrocytic maturation. All patients in this group received a "sprue diet," the parenteral or oral administration of liver extract, vitamin $B_{12}$ or folic acid, vitamin supplements, and, when indicated, soluble calcium and vitamin K. Of the 13 patients having nontropical sprue and normoblastic erythropoiesis, none experienced hematological or clinical improvement that could be attributed to the administration of any single hemopoietic agent or to a combination of these agents. Of the four patients with megaloblastic anemia, one failed to respond clinically and hematologically to the administration first of liver extract and subsequently to folic acid (50 mg. daily); the second showed an initial

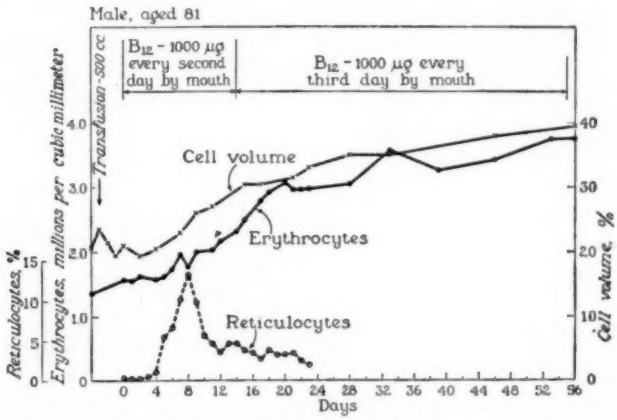


Fig. 1.—Hemopoietic response to oral administration of large doses of vitamin $B_{12}$ in the absence of intrinsic factor in a patient with pernicious anemia in relapse.

hematological response to the daily oral administration of 50 mg. of folic acid, only to relapse five months later despite continued administration of this compound; the third showed a moderate degree of improvement after the parenteral administration of liver extract; and the fourth patient improved clinically and hematologically after the intramuscular administration of vitamin $B_{12}$. The period of observation for the last two patients, however, did not exceed three and a half weeks.

The recent report of Taylor and co-workers [21] has stimulated interest on the effect of cortisone in nontropical sprue. Six patients in exacerbations of their disease were treated with this hormone, and all showed definite subjective and objective improvement characterized by diminution in the number of stools excreted daily, gain in strength and appetite, disappearance of abdominal cramping and distention, decreases in the amount of solids, water, fat, and nitrogen in the feces, increase in serum protein, and a return of prothrombin time to normal. These changes were interpreted as signifying more efficient intestinal absorption, although improvement in systemic metabolism also may have played a role. It is

interesting to note, however, that hematocrit readings, values for hemoglobin, and leukocyte counts were not altered significantly in three patients with anemia.

*Megaloblastic Anemia of Infancy.*—Although previously described, the importance of this form of anemia was not generally appreciated until Zuelzer and Ogden published an account of 25 cases in 1946.[22] The condition occurs in infants 2 to 18 months of age and is characterized by a normocytic or macrocytic anemia accompanied by megaloblastic regeneration in the bone marrow. It responds dramatically to the administration of folic acid [22] as well as to citrovorum factor [23] and to liver extract,[24] but responses to vitamin $B_{12}$ [25] have been variable. That the condition is not identical with juvenile pernicious anemia [26] is indicated by (1) the absence of histamine-fast achlorhydria in some cases, (2) the failure of relapse to occur after a short course of therapy with hemopoietic agents, and (3) the absence of peripheral neuritis or subacute combined degeneration of the spinal cord.

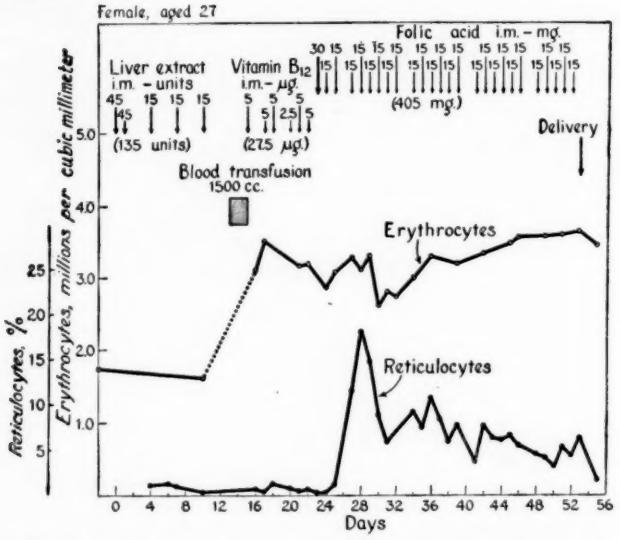


Fig. 2.—Absence of hemopoietic response to parenteral administration of liver extract and of vitamin $B_{12}$ and a prompt response to use of folic acid for megaloblastic anemia, which developed during the seventh month of pregnancy. Gastric analysis showed the presence of free hydrochloric acid.

Dietary deficiency and impairment of hemopoiesis by infection have been considered as etiological factors, the former probably being the more important. The condition has been observed most frequently among infants fed proprietary milk products low in protein content and ascorbic acid, the latter having been destroyed by processing procedures, and also among infants fed goat's milk [22] (including one patient in this series). In other instances, however, no evidence of dietary deficiency could be discerned.[27]

The studies of May and his associates [28] have shed considerable light on the disturbed metabolism associated with megaloblastosis of the bone marrow. They produced megaloblastic anemia in monkeys by means of milk diets deficient in folic acid and entirely devoid of ascorbic acid. Supplementing the diets with folic acid or folinic acid prevented or cured the megaloblastosis, even in the presence of severe scurvy. The administration of folic acid or folinic acid without the addition of ascorbic acid, or the use of ascorbic acid alone, promptly corrected the anemia. The administration of vitamin $B_{12}$, on the other hand, was totally without effect. The conclusion was drawn that the development of megaloblastosis in monkeys was due to a disturbance in the metabolism of folic acid caused by a deficiency of ascorbic acid and that the latter vitamin was required for efficient conversion of folic acid to folinic acid. This concept has received support from the investigations of Welch and co-workers.[29]

While there are similarities between the nutritional megaloblastic anemia of the monkey and the megaloblastic anemia of infancy, there are dissimilarities as well. The megaloblastosis of the monkey is corrected by the administration of ascorbic acid; that of the infant is not. [24b] Moreover, May and co-workers [24b] noted the development of megaloblastosis in the marrow of an infant with anemia and ascorbic acid deficiency after the deficiency of ascorbic acid had been corrected. At present, the pathogenesis of megaloblastic anemia of infancy does not appear to be established; however, available evidence favors the hypothesis that it is the result of a primary folic acid deficiency that is intensified or exaggerated by a deficiency of ascorbic acid. Ascorbic acid may serve to make folic acid or related compounds available by reversing the process that occurred when ascorbic acid was deficient. It is of interest that the incidence of megaloblastic anemia of infancy has diminished in frequency since 1948 when manufacturers of proprietary milk products began adding ascorbic acid in the amount of 50 mg. per reconstituted quart.[25a]

My colleagues and I had the opportunity of treating seven patients with megaloblastic anemia of infancy from 1946 to 1948. All infants responded promptly to treatment with folic acid and ascorbic acid. While megaloblastic anemia of infancy may be corrected by the administration of folic acid alone in doses as low as 0.2 to 0.5 mg. daily by mouth,[23] there is no apparent harm in administering larger quantities (15 mg. or more per day). Ascorbic acid in a dosage of 200 mg. a day also should be given. Crude liver extract (2.0 cc. daily) has been recommended,[28c] but the use of this product does not appear to be essential.

*Megaloblastic Anemia of Pregnancy and the Puerperium.*—During pregnancy or early in the puerperium an anemia distinct from the iron deficiency (hypochromic) or the physiological (normochromic normocytic) type of anemia may be encountered. The characteristic feature of this disorder is the finding of megaloblasts in the bone marrow. The picture presented by peripheral blood is not specifically diagnostic because either a normocytic or a macrocytic red blood cell pattern may be found.[30] In some cases, however, the blood picture may be indistinguishable from that of pernicious anemia, even to the finding of megaloblasts in stained films.[31] That the condition is not identical with pernicious anemia is manifested by the lack of response to the administration of vitamin $B_{12}$,[32] the absence of histamine-fast achlorhydria in the majority of cases, and the failure for relapse to occur after one course of treatment with folic acid. It should be remembered, however, that pernicious anemia may develop during pregnancy and that such patients not only respond to treatment with vitamin $B_{12}$ but require the usual maintenance therapy. I have observed one such case.

Megaloblastic anemia of pregnancy appears to be commoner in England than in the United States, judging from the number of cases reported in the literature from these two countries. It may develop at any time during pregnancy, but it is most frequently observed during the last trimester. It also is observed more commonly among multiparas than among primiparas. The cause is unknown. Dietary deficiency has been considered to be an etiological factor, at least in some cases, but the disorder has been observed in women ingesting adequate diets.[31] Another possible etiological factor, as yet incompletely elucidated, is the observation of Ungley and Thompson [32c] that rate of destruction of transfused erythrocytes is increased in women who have megaloblastic anemia of pregnancy.

In 1948, Bethell and associates [32b] demonstrated that megaloblastic anemia of the puerperium failed to respond to vitamin $B_{12}$ but that it did respond to folic acid. Shortly thereafter, my associates and I [31b] observed the same phenomenon in a patient with megaloblastic anemia of pregnancy. The hematological data are presented in fig. 2. These observations have been confirmed by others.[33] Reports of responses to extracts of liver have varied. Little or no effect has been observed from the administration of refined liver extracts, which are known to contain only traces of folic acid; however, significant hematological and clinical responses have been obtained from the oral or parenteral administration of crude liver extract or the oral administration of raw liver pulp,[31a] substances containing folic acid in amounts sufficient to stimulate hemopoiesis. Autolyzed yeast extract (marmite), reported first by Wills [34] and later by others as showing hemopoietic activity in megaloblastic anemia of pregnancy, also possesses folic acid in quantities sufficient to account for the responses observed. Whether or not some as yet unidentified substance (Wills' factor) possessing hemopoietic activity is present in yeast extracts remains to be determined, but present evidence favors the concept that folic acid is the active agent. Thus, although the cause of megaloblastic anemia remains obscure, it is apparent that the disorder is one of those conditions in which there is a disturbance in either the assimilation or utilization of folic acid.

*Association with Organic Disease or Surgical Procedures on the Gastrointestinal Tract.*—Gastric Lesions and Operations: Macrocytic anemia associated with carcinoma or polyposis of the stomach is rare. On the other hand, gastric polyposis or carcinoma is frequent among patients having pernicious anemia.[35] The incidence of macrocytic anemia among patients who have had gastroenterostomy or partial gastric resection is exceedingly rare in proportion to the number of such operations that have been performed. It is somewhat higher among persons in whom total gastrectomy has been done.[36] In most of the cases reported, however, studies of the bone marrow have not been made, so that data relating to the incidence of megaloblastosis following surgical procedures on the stomach are not available. In a review of my own cases, examinations of the bone marrow were made in seven patients (cases 2 to 8 of the table) seen at the Mayo Clinic from 1½ to 9 years after partial or total gastric resection. Pertinent data are given in the table. Three of the five patients subjected to partial gastrectomy had macrocytic anemia, but in none of these was megaloblastic erythropoiesis found. The two patients on whom total gastrectomy was performed are of special interest. One patient (case 7), followed for nine years after the entire stomach and 5 mm. of the duodenum had been removed, remained in good health. Hemopoietic agents were not administered during this period. The other patient (case 8), three years after a similar type of operative procedure for benign gastric ulcer with hemorrhage, experienced megaloblastic anemia indistinguishable from that of pernicious anemia. The hemopoietic response to the parenteral administration of vitamin $B_{12}$ is shown in fig. 3.

*Comparison of Type of Anemia and Type of Erythropoiesis Following Partial or Total Gastrectomy*

| Case | Age | Sex | Gastrectomy | Operative or Pathological Diagnosis | Onset of Anemia After Operation, Yr. | Type of Anemia | Type of Erythropoiesis in the Bone Marrow |
|---|---|---|---|---|---|---|---|
| 2 | 31 | F | Partial (10 cm. stomach; 1 cm. duodenum) | Duodenal ulcer | 1½ | Normocytic hypochromic | Normoblastic |
| 3 | 55 | M | Partial | Duodenal ulcer | 9 | Macrocytic hypochromic | Normoblastic |
| 4 | 37 | F | Partial | Duodenal ulcer | 5 | Microcytic hypochromic | Normoblastic |
| 5 | 64 | M | Partial (10.5 cm. stomach; 1 cm. duodenum) | Colloid adenocarcinoma, grade 3 | 2 | Macrocytic normochromic | Normoblastic |
| 6 | 55 | M | Partial (14 cm. stomach; 2 cm. duodenum) | Ulcerative adenocarcinoma, grade 4 | 4 | Macrocytic normochromic | Normoblastic |
| 7 | 52 | M | Total (entire stomach; 5 mm. esophagus; 5 mm. duodenum) | Ulcerative adenocarcinoma, grade 3 | 9 | None | Normoblastic |
| 8 | 68 | M | Total (entire stomach; 5 mm. esophagus; 5 mm. duodenum) | Benign gastric ulcer | 3 | Macrocytic normochromic | Megaloblastic |

Intestinal Lesions and Operative Procedures: Megaloblastic anemia may be encountered in the presence of intestinal strictures, gastrocolic and jejunocolic fistulas,[37] regional enteritis, and after intestinal anastomosis. Macrocytosis has been observed in a number of other disorders of the small intestine and colon (tuberculosis, carcinoma, and fecal fistula),[38] but in these cases examination of the erythropoietic pattern in the marrow was not made. Plum and Warburg [39] observed macrocytic anemia, termed by them "megalocytic anemia," in three

of four cases of regional enteritis, but no studies of bone marrow were reported. Cameron, Watson, and Witts,[40] in a review of the literature, found 61 cases in which intestinal stricture or anastomosis was associated with an anemia resembling pernicious anemia. In eight cases, including a case of their own, megaloblastosis was specifically recorded. In 24 of 44 cases in which gastric analysis was done, free hydrochloric acid was present in the gastric juice. The case reported by them is of special interest because megaloblastic anemia developed after a short-circuiting operation for regional enteritis that resulted in a blind loop of the distal part of the ileum of approximately 2 ft. (61 cm.) in length. At a second operation, multiple constrictions and distentions were found in the by-passed loop. The anemia responded to treatment with liver extract. Since free hydrochloric acid was present in the gastric juice of this patient, Cameron and his associates are of the opinion that megaloblastic anemia of intestinal origin is different from pernicious anemia, being due to stagnation of intestinal contents, probable change in intestinal flora, and the absorption of toxic substances, rather than to the absence of intrinsic factor. Laboratory evidence supporting their view has been reported by the same authors who observed the development of macrocytic anemia in rats following an operative procedure in which a blind loop in the small intestine was established. At the Mayo Clinic the development of megaloblastic anemia has been seen in two patients after the distal part of the ileum, cecum, and proximal part of the ascending colon had been removed for regional enteritis and in one patient in whom ileojejunal insufficiency developed following a similar operation for enteritis secondary to intestinal obstruction. One patient having regional enteritis responded satisfactorily to the parenteral administration of vitamin $B_{12}$ (fig. 5), and the other two improved on treatment with folic acid.‡ The hematological response in the patient with ileojejunal insufficiency is shown in fig. 4.

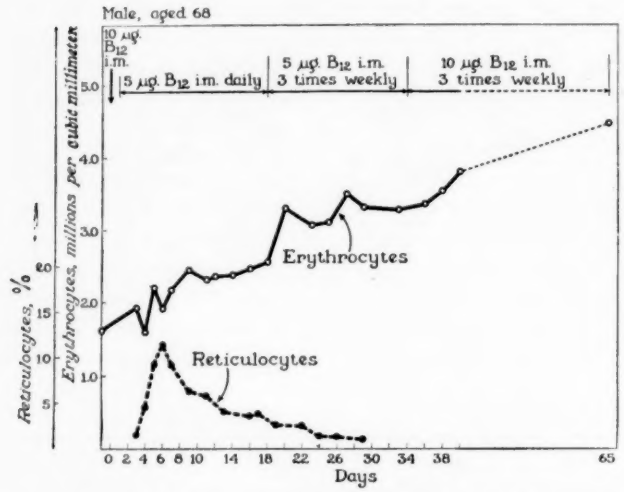


Fig. 3 (case 8 in the table).—Hemopoietic response to the parenteral administration of vitamin $B_{12}$. Anemia indistinguishable from pernicious anemia developed three years after total gastric resection (including resection of 5 mm. of the esophagus and 5 mm. of duodenum) for benign chronic hemorrhagic gastric ulcer.

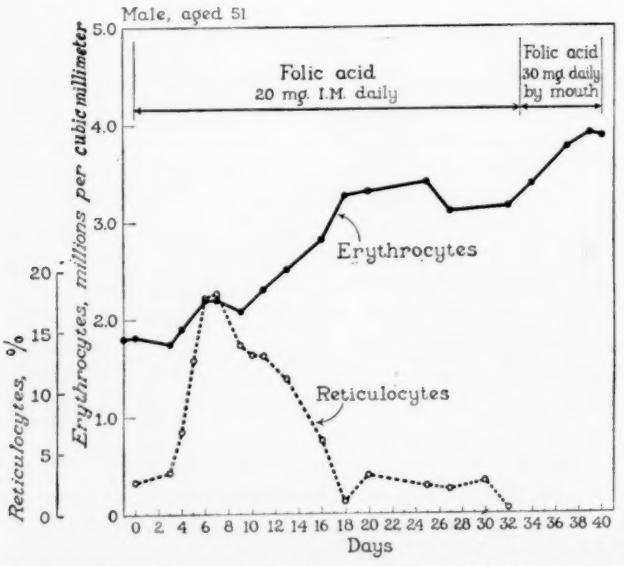


Fig. 4.—Hemopoietic response to the parenteral administration of folic acid in a case of megaloblastic anemia. The anemia developed two years after the distal 4 ft. of ileum, the cecum, and the right half of the colon had been removed and an end-to-end anastomosis had been performed for intestinal obstruction. An appendiceal abscess had been drained three years previously. At the time of admission, gastric analysis disclosed the presence of free hydrochloric acid; quantitative analyses of the stools for fat revealed that 63% of the dry weight of the stool was fat; the value for blood calcium was 8.7 mg. per 100 cc.; and the Quick prothrombin time was 20 seconds.

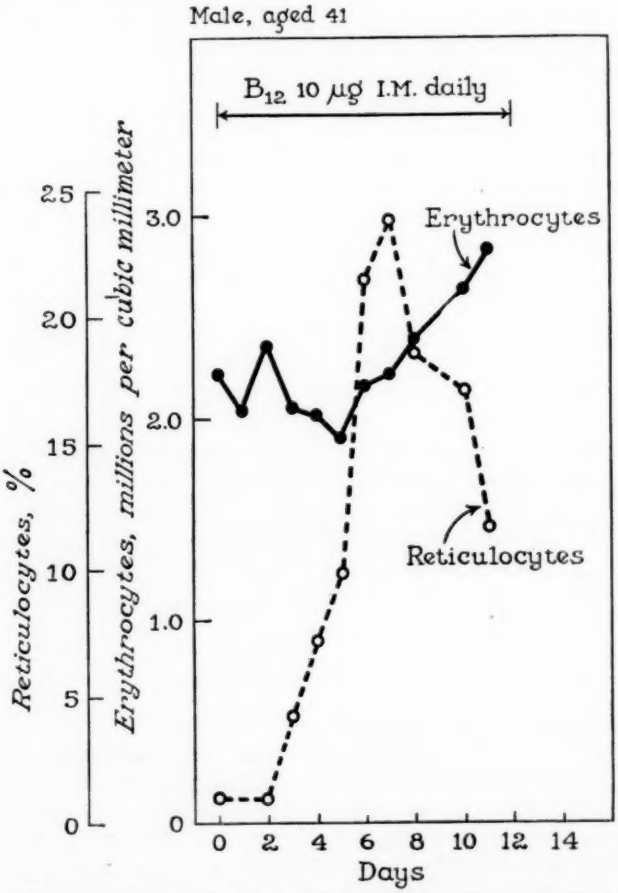


Fig. 5.—Hemopoietic response to parenteral administration of vitamin $B_{12}$ in a case of megaloblastic anemia associated with extensive regional enteritis of six years' duration. Five years prior to admission, 40 cm. of ileum, the cecum, and a portion of the ascending colon was removed and an end-to-end transverse ileocolostomy was performed. Relapse occurred three years later. Prior to instituting therapy with vitamin $B_{12}$, gastric analysis revealed a total acidity of 48 and free hydrochloric acid of 36.

‡ Folic acid for this part of the study was supplied by Lederle Laboratories Division, American Cyanamid Company, New York.

## COMMENT

While the clinical differentiation between iron deficiency anemia and other forms of anemia may be made with comparative ease, it is surprising how many patients continue to be treated with liver extract, hog stomach preparations, vitamin $B_{12}$, and folic acid when the only requirement is iron. Not only is needless expense incurred but the patient does not get well. In cases in which loss of blood has been eliminated as a cause and a nutritional basis for the deficiency has been established, the response to the oral administration of the bivalent form of inorganic iron often is dramatic. If iron cannot be tolerated when given orally or if the response to oral therapy is unsatisfactory, the intravenous administration of saccharated iron oxide affords a relatively inexpensive, easy, and effective method for correcting the deficiency.

Deficiency of iron does not cause an alteration in the pattern of erythrocytogenesis in the marrow, but a deficiency of either folic acid or of vitamin $B_{12}$, or of both, if sufficiently prolonged or severe, results in the development of megaloblastosis. Macrocytosis is the usual accompaniment of folic acid or vitamin $B_{12}$ deficiency, but normocytosis has been reported in some cases of megaloblastic anemia of pregnancy and of infancy. In view of this and the fact that macrocytic anemia associated with normoblastic erythropoiesis occurs frequently in chronic disease of the liver, detection of folic acid or vitamin $B_{12}$ deficiency rests primarily on the finding of megaloblasts in the bone marrow. Examination of the peripheral blood is a helpful but not a specific diagnostic tool.

Folic acid is present in foodstuffs in the form of conjugates, which are inactive until they are split by specific enzymes (conjugates) present in certain body tissues.[41] Recent evidence suggests that the "free" folic acid thus produced does not participate directly in the process of erythrocytic maturation but is converted to citrovorum factor (folinic acid), an enzyme facilitating the formation of pyrimidines such as thymine from amino acids. Conversion of folic acid to citrovorum factor takes place primarily in the liver and the kidney and to some extent in the bone marrow and is augmented in the presence of ascorbic acid.[42]

Vitamin $B_{12}$, which has been identified with Castle's extrinsic factor, also is abundantly distributed in foodstuffs (liver, beef muscle, eggs, milk and milk products, and glandular meats). A number of related but chemically distinct forms have been isolated from biological materials, which, in addition to vitamin $B_{12}$, include vitamin $B_{12}a$, $B_{12}b$, $B_{12}c$, and $B_{12}d$. Vitamin $B_{12}a$ and vitamin $B_{12}b$ probably are identical. The generic term cobalamin has been proposed for this group of compounds.[43] All of cobalamin analogues possess hemopoietic activity similar to that of vitamin $B_{12}$ when administered parenterally to patients with pernicious anemia.[44]

Deficiency of vitamin $B_{12}$ (or its analogues) develops when there is (1) an inadequate intake of the vitamin, (2) an absence of intrinsic factor in the gastric secretion, thus preventing efficient absorption and utilization of the small amount of the vitamin normally present in foodstuffs, or (3) when pathological organisms in the small intestine utilize the vitamin in such quantity that the host is deprived of it. Nutritional megaloblastic anemia is an example of the first type of deficiency, pernicious anemia is illustrative of the second type, and megaloblastic anemia due to infestation with Diphyllobothrium latum is an example of the third.[45] The reason for the development of megaloblastic anemia due to an apparent deficiency of vitamin $B_{12}$ in certain cases of regional enteritis (fig. 5) remains unexplained, but it may be related to increased utilization of vitamin $B_{12}$ by certain bacteria in the small intestine. Davis and Mingioli [46] have shown that Escherichia coli has an avidity for the vitamin.

The fact that total gastrectomy rarely results in the development of megaloblastic anemia is of special interest. If the human stomach were the only source of intrinsic factor, megaloblastosis would be inevitable after complete removal of this organ. The rarity with which such a complication occurs suggests that intrinsic factor may be produced in the small intestine of the human being, possibly the duodenum, as well as in the stomach, but there is little experimental evidence to support this hypothesis. Activity of intrinsic factor has not been found in duodenal secretions devoid of gastric juice,[8b] but some activity has been noted in duodenal mucosa.[1c]

Megaloblastic anemia associated with intestinal dysfunction or disease and megaloblastic anemia of infancy and of pregnancy appear to be predominantly due to a deficiency of folic acid. This type of deficiency presumably bears no relationship to the presence or absence of intrinsic factor, since it occurs in patients having hydrochloric acid in their gastric secretions. It seems rather to be due to faulty absorption from the gastrointestinal tract, to defective diets, or to a combination of these two factors. Ascorbic acid deficiency also may be a contributory cause by restricting the formation of citrovorum factor from its precursor, folic acid.

With the exception of nontropical sprue, treatment of the megaloblastic anemias is a comparatively simple matter. Pernicious anemia requires the use of liver extract or vitamin $B_{12}$, preferably given parenterally, but folic acid should not be administered because of the risk of hematological relapse and the development or progression of neurological manifestation of the disease. Liver extract or vitamin $B_{12}$ also should be employed in cases of megaloblastic anemia occurring after total gastric resection. The use of folic acid is indicated in megaloblastic anemia associated with intestinal dysfunction or disease and in megaloblastic anemia of infancy and of pregnancy. The simultaneous administration of ascorbic acid in this group of diseases, and particularly in megaloblastic anemia of infancy, would appear to be advisable. For the rare patient failing to respond satisfactorily to the administration of folic acid, treatment with vitamin $B_{12}$ should be instituted. Very rarely, a dual deficiency of vitamin $B_{12}$ and folic acid may exist, thus requiring the administration of both vitamins.[43] There is no evidence at present that folic acid is harmful to tissues of the nervous system when a deficiency of vitamin $B_{12}$ does not exist.

The problem of therapy in nontropical sprue is complicated by impairment of absorption in the alimentary tract of multiple nutrients in food. Hence, it is not surprising that the administration of liver extract, vitamin

$B_{12}$, or folic acid does not relieve the patient of manifestations of the disease that are unrelated to the deficiency of hemopoietic substances. The observation of Taylor and his associates [21] that the administration of cortisone facilitates intestinal absorption during acute exacerbations of the disease appears to be a contribution of considerable importance; however, since Taylor and associates did not find significant alterations in the hematocrit readings or in values for hemoglobin following treatment with cortisone, the continued use of hemopoietic agents would appear to be indicated in this disease.

SUMMARY

On the basis of my experience, nutritional anemia appears to be comparatively rare in the North Central part of the United States. It is seen less frequently as a result of the inadequate intake of food than as a consequence of faulty absorption and assimilation from the gastrointestinal tract of hemopoietic factors normally present in food. This may occur in a variety of disorders. Clinical experiences with the newer hemopoietic agents in a number of these disorders and the indications for their use have been enumerated.

909 Hyde St. (9).

# CARDIAC SURGERY IN A COMMUNITY GENERAL HOSPITAL

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*and*
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The advances in cardiac surgery during the past several years constitute one of the great contributions of medicine to man's welfare and have ushered in a new era of cardiology. The procedures devised by Strieder, Gross, Grafoord, Blalock, Potts, Sellers, and Brock for the relief of congenital cardiac malformations and by Beck and Bailey for acquired lesions have been of tremendous benefit to hundreds of patients. The work of these men and their associates has established a tremendous volume of investigation, experimental and clinical; and physicians have been forced to change many concepts of the pathological physiology, the natural history, and, most important, the prognosis of various types of heart disease. Instead of an early death or, at best, a life of invalidism, a multitude of patients subjected to heart and great vessel surgery have been given new hope and the physical wherewithal for extended years.

Unfortunately, however, owing to the nature of these operations, their benefits are not yet available to all patients suffering with the lesions they are designed to remedy. The surgical procedures developed in medical centers have been, for the most part, confined in application to these centers. Dissemination of knowledge of the special techniques, surgical and diagnostic, has taken place in two ways: through the training of residents and fellows at these institutions and through the observation of procedures by experienced men from other institutions. Thus, facilities have become more widespread, but the tendency, nevertheless, has been toward a concentration of talent in teaching hospitals. This has been of small moment to persons with the means to afford travel to, and the sometimes prolonged stay at, such centers or to those fortunate enough to secure the aid of local charitable, business, or benevolent groups. To those without such means or sponsorship, help and hope must be deferred to an uncertain future.

Many such patients were known to live in New Jersey. It was estimated that there were at least several hundred persons in the state who could be benefited by surgical procedures but who were unable to afford the necessary expenses to travel to a center in a neighboring state. The seriousness of the lack of local facilities was particularly apparent to those physicians associated with the medical and pediatric staffs of this hospital. Through their clinics and offices each year a large number of patients passed who were afflicted with remediable cardiac lesions. Only a small percentage of these patients were able to take advantage of the help offered outside the state. How to aid the majority was the subject of numerous informal discussions among staff members. It became apparent that the solution to the problem lay in developing at this hospital the necessary facilities for definitive studies and surgery. To accomplish this in a community hospital presented several great difficulties, the most important being those of space, finances, and personnel.

Fortunately, the administration and the general staff, eager to extend the services of the institution, were willing to underwrite the expense of developing a suitable program. They agreed to convert sufficient space from its current use to a cardiorespiratory laboratory, to provide much of the needed equipment, and to assume the hospitalization costs for those who could not afford them. The medical personnel required for instituting and maintaining the project was adequate. There were on the staff well-trained cardiologists, pediatricians, physiologists, and roentgenologists whose participation was assured; however, surgical personnel remained a problem. Two staff surgeons were especially enthusiastic about the proposed program: one trained in and confining himself to thoracic surgery, but with little experience in cardiac work, and the other a general surgeon. To utilize their abilities one of two courses lay open: to have one or both temporarily give up an established practice and gain the necessary special skills at a residency or fellowship level or make some arrangement whereby the requisite training could be secured at this hospital. At this point the advice of Dr. Charles P. Bailey of Philadelphia was sought. After several conferences with him a satisfactory answer to the problem was resolved. He agreed to spend one day each week at this institution in a teaching capacity. Dr. Claude

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S. Beck of Cleveland was invited to devote one or two days a month for further instruction. In addition, it was arranged that the surgeons would devote one day each week to studying in the experimental cardiopulmonary laboratory at Hahnemann Medical College. Four surgeons are now fully trained to do cardiac surgery.

There followed many hours of planning on the part of those persons interested in the project. It became apparent early that a hard-and-fast decision must be made as to whether or not this would continue to be a group effort, with each qualified man in the group having a voice in determining how a patient should be studied and what should be done for him. The alternative was for the individual clinician who would first see the patient to decide on the proper work-up and, in conference with the surgeon, on disposition. The unfortunate features of the first proposition were obvious: delay, added expense of time and money, and possible indecision in some cases in which definitive action should be taken immediately; however, the alternative was not more attractive. In a group composed, on the whole, of men with little familiarity with the problems of cardiac surgery, the combined would be preferable to the individual decision until such time as each man had gained a degree of knowledge of the multitude of factors involved. Too, it was feared that what had started as the unselfish contributive undertaking of many might, if it did not remain in the province of the group, fail as the result of evolution of selfish forces. Nobler ventures in this manner have perished. It was eventually agreed that all major decisions in regard to a patient would be arrived at as a result of conference among all those involved: cardiologists, pediatricians, roentgenologists, physiologists, surgeons, and the practitioner who would refer the patient.

Shortly after the initiation of the program, the interest of Dr. Daniel W. Bergsma, commissioner of health of New Jersey, and that of Dr. Marion R. Stanford, chief of the heart section of the New Jersey State Department, was aroused, and in a few weeks financial aid of their organization was assured for some of the equipment but not for service care. This would entail great sums of money, which were not available. State funds were made available for equipment and for a teaching program that would affect, directly and indirectly, all patients with cardiac disease in the state. In order that the money furnished would do the greatest good for the greatest number, it was pointed out that the newer knowledge of cardiology and of cardiac surgery should and must be made available to all physicians in the state. To that end a course in practical cardiology was developed, opened to all interested physicians, and centered around the already functioning project at this hospital. A prospectus of such a course was drawn up. This consisted of lectures by prominent cardiologists, ward rounds, instruction in roentgen interpretation and electrocardiography for small groups, demonstration of pathological specimens, and an opportunity for active participation in the work of the clinics and for observation of cardiac surgical procedures. Thus, an over-all view of cardiology could be gained.

In the first 24 months of operation of this program, from January, 1950, to January, 1952, 1,582 new patients were admitted to the hospital for cardiac treatment and evaluation. These cases represented all types of cardiac diseases, including coronary disease, congestive heart failure, rheumatic heart disease, congenital heart disease, hypertensive heart disease, and arteriosclerotic heart disease. There were 562 new patients referred to the cardiac clinic, 304 of whom were referred by private physicians and 158 by social agencies and hospital clinics. A total of 411 were admitted to the hospital for evaluation and diagnostic work-ups, which included cardiac catheterization, aortography, and angiocardiography. A total of 104 patients underwent surgery, which included mitral commissurotomy, Brock's operation, patent ductus arteriosus, coarctation of the aorta, and Beck's operation. Although only 104 patients have been operated on up to January, 1952, it must not be concluded that only this number were candidates for operation; many more were scheduled for a future time. In fact, from January, 1952, to the present time, the number of cases has been doubled and is increasing with each succeeding month.

All clinic patients come to consideration through one of the two cardiac clinics maintained at the hospital. One is the rheumatic fever and congenital heart clinic, financed by funds of the New Jersey Crippled Children Commission, and designed primarily for the care of children with rheumatic heart disease and congenital cardiac anomalies who reside in Essex County. The other is the general cardiac clinic to which any patient may come for help and to which any physician may refer a patient for study. Private patients may be referred by their physicians to the cardiologists or pediatricians. The basic work-up for each patient is the same: a history and physical examination, x-ray examination and fluoroscopy with barium swallow, and an electrocardiogram with unipolar limb and V leads. Following these studies, any patient considered to have a remediable lesion or a lesion undiagnosable with certitude by ordinary clinical and roentgen means is referred to conference. This conference is held weekly, the same day surgery is performed and the cardiology course is in session. Here the evidence gathered in the clinic is presented. Each member of the group has the opportunity of examining the patient, viewing the roentgenograms, and studying the electrocardiogram. Should one wish to check the fluoroscopic findings this may be done in a nearby room. Following discussion of the available information, a decision as to further studies, particularly angiocardiography, aortography, and cardiac catheterization, is made. In congenital lesions only those patients whose conditions are too critical to allow the slight risk come to surgery without one or more of these diagnostic procedures having been performed. We are of the opinion that it is much better for the patient, the surgeon, and all concerned if an exact anatomic diagnosis is made beforehand. In the case of acquired lesions, preoperative and postoperative cardiac catheterization is performed whenever possible.

An appointment for the desired study is made, and after it is completed the patient is dismissed to be presented again at a future conference. If the anatomic diagnosis is apparent, the decision as to disposition of the patient is made. The internist, rather than the surgeon, has the determining voice. If surgery seems in order, the procedure is scheduled. At the conference on that day the

operative findings are discussed. At intervals thereafter the patient's progress is assessed by the conference group.

The cardiology course given during these past two years has been a success. Authorities from Philadelphia, New York, and Washington have given a series of 20 two hour lectures. The courses were announced to the profession and the physicians of the state invited, 720 physicians signifying their desire to enroll. Only 80 physicians could be accommodated, and this number of applicants was accepted. Attendance at the lectures was very gratifying. Many physicians availed themselves of the wider opportunities and arranged to spend the entire day at the hospital in close contact with patient material. After several weeks these physicians expressed a desire for additional practical teaching, and another morning of clinical work was arranged for their benefit. Since then, two more courses have been given and also an advanced course in clinical cardiology for those who have taken the general course. The last classes consisted of 120 physicians from the entire state for the general postgraduate course and 50 additional physicians for the advanced clinical course.

### COMMENT

Several lessons have been learned during the evaluation of this project: 1. Given sufficient enthusiasm and interest on the part of a hospital administration and staff, great advances may be made. The success of the project demonstrates that extraordinary medical care can be made available to all who are needy if physicians are willing to make sacrifices in their behalf and if all other groups such as the department of health and the women's auxiliary of the hospital can be stimulated to help them. 2. The disposition of patients by group conference serves the patient best. It may be accepted as true that the number of surgical procedures, of mistaken diagnosis, and of instances of gross mismanagement of patients would fall sharply were such a system to become generally used in every hospital department for all patients. 3. The spread of techniques and knowledge by leaders from the medical center to the community hospital need not take years, as is so often the case, but can be accomplished in a relatively short time if the hospital and its staff are sufficiently aggressive in seeking the help of these leaders. Medical education on the postgraduate level is only partially successful when served just by lectures, by short intensive courses, or by medical meetings. It is education of the highest order when the teacher comes to the workshop frequently and serves as a constant source of stimulus. By this means other teachers are made and knowledge is continually spread. 4. It is our impression that such a program has made a definite contribution to the welfare of the patient, to the physician, and to the community in general.

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# BALLOON TECHNIQUE IN THE CYTOLOGICAL DIAGNOSIS OF GASTRIC CANCER

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*and*
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Efforts to obtain material from the stomach that would be suitable for the cytological diagnosis of gastric cancer started in this laboratory in 1946.[1] Among the early cases there was a patient with a small gastric lesion that was thought to be an ulcer. Gastric smears obtained by simple aspiration with a Levine tube showed many groups of malignant cells. This single early success was very important, for it formed an optimistic background for many discouraging studies that were to follow. During the next three years over 1,000 patients were examined, using a variety of washing techniques. About the best accuracy that was obtained in these efforts was 60%.[2] In nearly half of the cases of gastric cancer we failed, by any of the methods tried, to obtain suitable material for cytological interpretation.

In 1949 these washing methods were abandoned in favor of an abrasive balloon technique that had been devised. During the first year of trial with the balloon device, the studies were confined to patients in whom the pathology was known.[3] This was necessary because it was essential to learn at the outset which portion of the material obtained by using the balloon was likeliest to contain well-preserved groups of cells. It was necessary to learn which was the best material: that aspirated while the balloon was in the stomach, that on the balloon after it was removed, or that which remained in the stomach after the balloon was withdrawn. To get this essential information is was necessary to do rather extensive comparative studies in each patient—a procedure that was quite impractical to carry out as a routine diagnostic measure. From this first year of study it was observed that the best cell groups were usually found on the balloon itself. When gross particles of tissue were visible on the balloon they were smeared separately. The remaining material was washed off the balloon in Ringer's solution. The material aspirated while the balloon was inflated was also very good, though generally a little less reliable than that found on the balloon. With this background it was then

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Associate Professor of Clinical Surgery (Dr. Cooper) and Professor Emeritus of Clinical Anatomy (Dr. Papanicolaou), Cornell University Medical College, and Assistant Attending Surgeon (Dr. Cooper), New York Hospital.

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possible to test the new technique on unknown gastric diagnostic problems. This report is based on the first 238 cases in which the balloon technique has been so tested.

## MATERIALS

The patients studied were inpatients on the pavilion services of the New York Hospital. The patients selected were those with gastric diagnostic problems that were thought likely to require surgery. Care was taken to exclude any patients with marked recent gastrointestinal bleeding and patients with cirrhosis of the liver and possible esophageal varices. No bleeding of any clinical significance was encountered in over 300 clinical trials with the apparatus, and it is felt to be reasonably safe to use within the limitations mentioned. The specimens were collected by a technician, who prepared the smears and evaluated them as to quality on the same day. If the material was unsatisfactory for cytological evaluation, he obtained another specimen the next day or as soon as the patient could be prepared. In most cases the first smear was satisfactory, but the occasional patient with gastric retention required further preparation to rid the stomach of retained debris. The smears were read and evaluated by the cytologist, who had no clinical information whatever to influence his interpretation. The cytological reports were then compared with the final diagnosis, which is established beyond reasonable doubt in this group of patients.

The apparatus consists of a 16 French double-lumen tube 100 cm. in length with marks at 45, 60, and 75 cm. (fig. 1). One lumen is connected proximally to a syringe and distally to a perforated bucket. The other lumen is connected proximally to an inflating bulb and distally to a balloon. The balloon is made of a condom open at both ends. Around the balloon is fitted a fine netting, and the ends of the balloon and netting are tied to the distal end of the double-lumen tubing at points 8 cm. apart. When deflated the balloon and netting collapse on the side of the tube; when inflated with 175 cc. of air the balloon measures 10 by 5 cm. The apparatus used in the first experimental series [3] attained its abrasive quality from a series of about 200 silk knots that were tied to the outside of the balloon. In the present series of cases the silk knots are replaced by an enveloping veil, which is fashioned from black silk veiling that is readily available in department stores. The specimens are as good or better in the later series, and the balloon is much easier to make and maintain.

## PROCEDURE

The test is done in the morning, all food and fluid being withheld for the previous eight hours. This is usually sufficient preparation, but if the patient has gastric retention or has had barium the day before it may not be adequate. If the stomach is found to have retained food particles, any quantity of fluid, or barium, the test should be abandoned for that day and the stomach further prepared. A day of liquid diet followed by a thorough lavage the night before will be adequate in all cases except those with marked gastric retention. In such cases several days of a liquid diet followed by nightly lavages or continuous aspiration the night before may be necessary to clear the stomach of all retained debris. This is emphasized because the most essential factor in obtaining good specimens is a clean dry stomach. All dentures are removed, the mouth is rinsed, and the patient is instructed to expectorate all saliva. The deflated balloon is wet in Ringer's solution and passed orally, with small sips of the same solution taken through a drinking tube. Most patients swallow the balloon easily. If any great difficulty is encountered the gag reflex may be suppressed by a little 2% solution of tetracaine (pontocaine®) hydrochloride spray.

When the tube is past the 60 cm. mark the balloon is in the stomach. The stomach is then aspirated until dry, and this material is saved for the fasting specimen of a gastric analysis. Histamine is then given, and three 10 minute specimens are collected for gastric analysis, using the continuous aspiration technique. After 30 minutes of aspiration the stomach is clean and dry. The balloon is then inflated with about 150 cc. of air, and the tube is withdrawn until the balloon is checked at the cardia. When at the cardia, the inflated balloon will not come up any further and the patient may gag. Peristaltic action

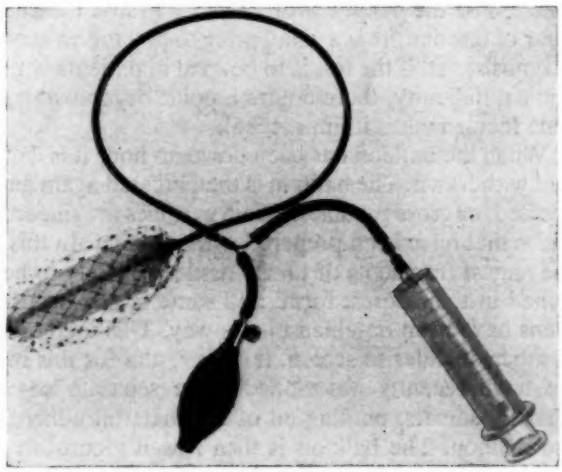

Fig. 1.—Apparatus used in cytological test.

then carries the balloon down to the pylorus in 5 to 10 minutes. The balloon is deflated, reinflated, and pulled back to the cardia while inflated. This process is repeated five or six times over the period of 30 minutes. While the balloon is down the stomach is kept dry by frequent aspiration. This material is usually discarded but is saved for processing in cases when the examination is being repeated, for it often contains very well-preserved groups of cells. It may also be saved and processed if the material on the balloon is scanty. The guiding factor in this regard is the practical one of keeping the number of smears down to a maximum of four or five and still have on these slides as much good material and as little debris as possible. It may be wise in some cases to pool the material. If the aspirated material is saved, it should be put into 95% alcohol as it is collected. The material aspirated while the balloon is inflated is often slightly pink and may contain fresh red blood. It is likelier to contain fresh blood if a gastric lesion is present. If the amount of blood is in any way alarming the test should be terminated. There has been no gastric hemorrhage or untoward reaction in over 300 clinical trials with the balloon method, though some

fresh blood has been obtained in a number of cases. The time of 30 minutes to leave the inflated balloon in the stomach has been selected arbitrarily. In a number of cases the time has been reduced, and these specimens have been perfectly adequate. In a recent case with a friable papillary carcinoma an excellent specimen was obtained in 10 minutes. While it is obvious that in the papillary types of gastric cancer the procedure may require less than one-half hour, experience alone demonstrates what the optimum time is for the disease as a whole. For the patient with a serious gastric disorder an hour of discomfort is a small price to pay for an accurate diagnosis; yet, if the test is to be used in patients with less clinical difficulty, there comes a point beyond which the time factor makes it impractical.

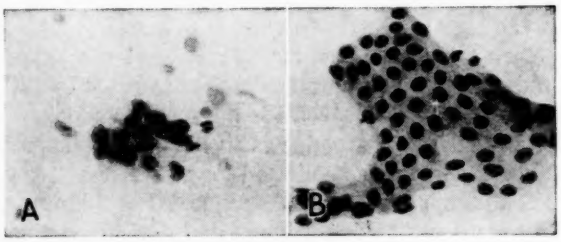


Fig. 2.—Photomicrographs showing clusters of normal gastric cells. Note regular pattern and uniformity of nuclei in *B* (× 300).

When the balloon has been down an hour it is deflated and withdrawn. The balloon is then inflated again and inspected for gross particles. These particles are smeared on slides that have been prepared with albumin. In this way the largest fragments of tumor tissue are likely to be obtained in their purest form, and some of our best specimens have been obtained in this way. This increases the number of slides to screen, however, and for this reason we have recently abandoned these separate so-called "pinch" smears, pooling all of the material adherent to the balloon. The balloon is then rinsed vigorously in a 40% solution of Ringer's solution and alcohol. This puts into suspension the particles clinging to the net. The solution is then centrifuged for 30 minutes at 1,500 rpm and the sediment smeared on two to four slides, depending on the quantity of sediment. The smears are then fixed and stained according to the Papanicolaou technique.[4] Once the smears are fixed, delay is not important, but the material should not be allowed to stand around for more than an hour at any stage before fixation.

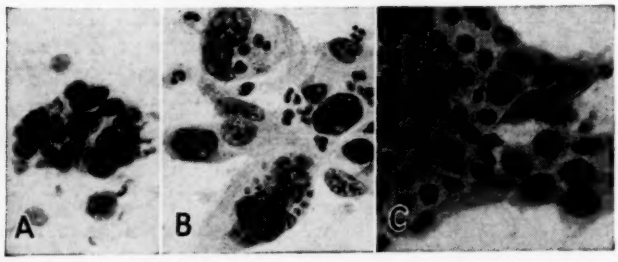


Fig. 3.—Photomicrographs of smears taken from three adenocarcinomas (× 330). *A*, malignant cells showing crowding, nuclear enlargement, and hyperchromasia, *B*, malignant cells showing extreme nuclear abnormalities, and *C*, malignant tissue from edge of tumor showing both normal and cancer cells.

4. Papanicolaou, G. N.: New Procedure for Staining Vaginal Smears, Science 95: 438-439 (April 24) 1942.

## CYTOLOGICAL MATERIAL

The smears thus obtained and processed then go to the cytologist for interpretation. The gastric mucosa is fairly resistant to the abrasive action of the balloon, and the material obtained from a normal stomach is likely to be scanty. A fair number of small and occasionally large clusters of normal gastric cells are seen, however, and they are usually relatively easy to interpret as such (fig. 2). More cells and groups of cells are usually encountered in specimens from stomachs containing an ulcer or a growth. It is the interpretation of these abnormal cells that calls for the greatest skill and judgment on the part of the cytologist. The criteria for malignancy of these cells and cell groups have been discussed in detail elsewhere.[3] It is sufficient to say that the material obtained from the balloon technique is well enough preserved to attain a high degree of accuracy in its interpretation and that it is immeasurably better than the material obtained by the original lavage techniques (fig. 3).

The smears are read as class 1 or 2, which are considered negative, class 3, which is suspicious, and class 4 or 5, which are considered positive. The table shows the correlation between the cytological interpretations and the final diagnosis. Most of these patients were suspected at one time in their diagnostic work-up of having gastric cancer, which was the indication for doing the test. In many cases the smear was done before the x-ray examination. All of the tests were done before operation. Finally, 46 patients proved to have gastric cancer, 4 lymphosarcoma of the stomach, and 1 cancer of the esophagus: a total of 51 cases with malignant disease involving the upper gastrointestinal tract. The remaining 187 cases proved to have benign gastric ulcer, gastric polyps, or other diseases with either normal stomachs or no malignant gastric lesion.

*Correlation Between Cytological Reports and Final Diagnosis in Patients with Gastric Diagnostic Problems*

| Diagnosis at Operation | Reports of Balloon Test | | | | | Total Cases |
|---|---|---|---|---|---|---|
| | Class 1 Negative | Class 2 | Class 3 Suspicious | Class 4 | Class 5 Positive | |
| Malignant | 4 | 2 | 7 | 9 | 29 | 51 |
| Nonmalignant | 103 | 74 | 9 | 1 | 0 | 187 |
| | | | | | | 238 |

*False Positive Case.*—It will be noted in the table that one case was given a class 4, or positive, report that proved at operation not to have gastric cancer. This patient had cirrhosis of the liver with ascites and was thought clinically to have gastric cancer. The stomach was palpated but not opened. The patient has been followed for eight months, and it seems likely that the diagnosis of cirrhosis is correct. The slides have been reviewed and still contain highly suspicious cell groups. There is no apparent explanation for this 1 false positive case in 238 clinical diagnostic problems.

*False Negative Cases.*—Class 1 or 2 reports were given in six cases that subsequently turned out to have malignant lesions. These are clearly missed diagnoses and are listed in detail in order to clarify the limitations of the smear technique. One of these patients had a small narrow stenosing lesion in the most distal portion of the antrum. It was probably not reached by the gastric balloon. The specimen was quite acellular. Another had a

2 mm. carcinoma in situ in the border of what appeared to be a benign gastric ulcer. This lesion was found by the pathologist only on recutting of further sections, which was prompted by a positive smear taken directly from the cut surface of the operative specimen. Another had a lymphosarcoma with a necrotic membrane over its surface. The last three cases were all fairly large tumors with deep ulcerating craters. In all of these the infiltrating tumor was submucosal with normal gastric mucosa up to the edge of the crater. No viable cancer cells reached the surface of the gastric lumen. It seems likely that these six cases are absolute limitations for any surface biopsy diagnostic method and that all such cases are likely to be missed by this technique. Such cases are uncommon in gastric cancer, however, and should not greatly limit the accuracy of the method in the disease as a whole.

*Suspicious Cases.*—Class 3, or suspicious, reports were given in nine cases that proved not to have cancer. Two of the specimens contained numerous clusters of cells that did not appear malignant, yet were not normal. One of these was diagnosed cytologically as a gastric polyp, and both turned out to have benign gastric polyps at operation. These are not, therefore, errors and are not false reports, for the cytological readings were a true reflection of the pathological condition found at operation. Of the remaining seven patients that did not prove to have cancer, yet were given suspicious reports, the final diagnosis was benign ulcer in five cases and normal stomach in two cases. In the five cases of ulcer removed surgically the pathological diagnosis was made on sample sections rather than serial sections. The possibility of minimal malignant change cannot, therefore, be ruled out. Seven cases that proved to have malignant lesions were given suspicious, or class 3, reports: six were gastric cancers and one was a lymphosarcoma. In retrospect some of these might be read now as class 4, or positive; yet they were not so interpreted preoperatively. While these suspicious reports pose something of a problem for the clinician to interpret, their occurrence in only 16 of the 238 cases in this series does not appear to be a serious limitation of the method as a whole. Seven of these suspicious cases turned out to have malignant disease, two others had gastric polyps, and in the final analysis only seven of the cases given suspicious reports turned out to have stomachs free of a neoplasm. Five of these had benign ulcer for which gastric resection was clearly indicated, and only two cases had no gastric disease. Though one would hesitate to interpret suspicious reports as positive, for practical purposes, so far in this series, such an interpretation would be nearly justified. Some of the dilemma presented by the class 3 reports can certainly be clarified by repeated specimens in such cases. When repeated specimens are necessary, it is important to save and process all of the material obtained from the stomach while the balloon is down, in order to give the cytologist as much material as possible for interpretation. Whether this material should be pooled or smeared separately is a question. The guiding principle in this regard will depend to some extent on the quantity of sediment obtained for smears. If this quantity is great it should probably be smeared on separate slides, but if it is scanty it may be more practical to pool all of the material obtained onto two to four slides.

*Positive Smears.*—In 38 of the 51 cases that proved to have malignant disease, the smears were clearly positive. If the 7 suspicious reports are also interpreted as evidence of a positive diagnosis, which seems somewhat justified in this series, this technique has been accurate in detecting gastric cancer in 45 of the 51 cases, or 88.2%. It is significant that in 29 of the 51 cases, class 5, or strongly positive, reports were rendered, with only 9 class 4 and 7 class 3 reports. It is not uncommon in the positive smears to find cells with mitotic figures in the nuclei (fig. 4). This finding not only gives indisputable evidence of proliferative activity but also gives some idea about the state of preservation of the cells obtained by the balloon technique. Mitotic figures were never seen in the smears obtained by the older lavage techniques, not because they were absent but because they could not be recognized in their state of poor preservation.

Fig. 4.—Two cancer cells showing abnormal mitoses. Final diagnosis was adenocarcinoma (× 600).

*Negative Smears.*—In the 187 cases that had benign gastric disease or normal stomachs, the smears were clearly negative in all but 10 cases. One of these was a frank error, two were accurate reports because the patients proved to have benign polyps, and seven were suspicious reports in negative cases. If the suspicious reports are considered errors, 179 of the 187 cases had accurate reports, or 95.7%. The negative smears are usually readily recognized as such. Most of them are quite accellular, and the cytological material is scanty compared with that of the positive smears. The normal cell groups, when present, are usually easily identified.

*Lymphosarcoma.*—Four of the patients in the series proved to have lymphosarcoma of the stomach. The smears in two of these were reported as class 5 with a specific diagnosis of lymphosarcoma because of many malignant cells that appeared to be of lymphoid origin. Another was read as class 3 and suspicious of lymphosarcoma. The fourth case was missed (one of seven frank errors in the entire series), being given a class 1 report. In retrospect this last case does show some highly suspicious lymphoid cell groups.

### OVER-ALL ACCURACY AND LIMITATIONS

If the suspicious reports are ignored in the series, there were 7 frank errors in the 238 diagnostic problems, an over-all accuracy of 97.1%. Regardless of how the suspicious reports are interpreted, it is apparent that this technique offers a diagnostic method with an accuracy that far exceeds that of any other method available at the present time. In this same series of cases, the accuracy of the x-ray examination was about 85%, if false positive and missed x-ray diagnoses are included. In the first 100 cases, 4 cases with cancer were interpreted by roentgenography to have benign lesions and 11 cases with benign lesions were interpreted as malignant. Though the balloon smear technique is certainly more accurate than the x-ray method in the interpretation of lesions, it does not take the place of the x-ray examination in gastric diagnosis. A negative smear does not make a diagnosis of gastric ulcer, nor does a positive smear give any concept of the location or the extent of the gastric cancer.

Some comment should be made on the difficulties and limitations of this diagnostic method. From the clinical point of view the test is relatively easy to perform and is not too difficult for patients. Adequate cytological material does require strict adherence to a few simple details. 1. The stomach should be absolutely free of all food, fluid, and debris, a condition that is not always easily attained in patients with gastric retention and may require several days of preparation. 2. The specimens obtained should be intelligently handled in regard to pooling of the various fractions, i. e., that obtained from aspirating while the balloon is inflated and that rinsed off the balloon after it is withdrawn. 3. There should be minimum delay in the processing until the material is fixed on the slide. Observance of these details can most easily be accomplished if a technician can be trained who takes the specimens, processes them, and screens the smears as to quality. It is difficult to train an ever-shifting house staff to take care of these details.

A more important limitation of this method is the availability of trained cytologists to interpret the smears. It is felt that this has been accomplished in our laboratory, where the cytological staff has had five years of experience in reading gastric material. Cytologists with less background and particularly those new in the field of cytology can be expected to have more difficulty in reading the smears; however, reasonable accuracy can be attained with adequate training. The technique can be learned with some facility, and others trained in the field may well surpass the accuracy attained in this series.

### COMMENT

There were two cases in this series that had roentgenograms interpreted as normal that had positive smears and proved to have gastric cancer. One of these deserves mention. It was that of a man of 74 who was hospitalized because of anginal pain and in the course of work-up was found to have occult blood in the stools. Four gastrointestinal series in two different hospitals were negative, and no lesion could be seen on gastroscopy. Two smears using the balloon technique were strongly positive. At operation a large inoperable cancer of the upper half of the posterior wall of the stomach was found. Though it did this patient little good to discover the gastric lesion before it was found by roentgenogram, the case emphasizes the great need for more sensitive and accurate diagnostic methods in gastric cancer.

Very little is known regarding the value of this technique in the early diagnosis of gastric cancer, because about two-thirds of the cases seen are inoperable and really small gastric cancers are a rarity. Three of the cancers in this series were lesions less than 1 cm. in diameter, and two of these had strongly positive smears. The only small lesion that was missed cytologically was a carcinoma in situ 2 mm. in diameter, which was discovered only by serial section of what appeared to be a benign ulcer. This scanty evidence suggests that the method may be accurate in the detection of early gastric cancer. The testing of this theory will have to await the application of the balloon smear technique to groups of patients in the presymptomatic, or at least early symptomatic, phases of the disease. This proof will not be come by easily or quickly, but as the method becomes more widely known and generally used it is felt that some cases of gastric cancer will be discovered in their earlier phases. Earlier diagnosis cannot help but result in more cures of this disease.

### SUMMARY

1. An apparatus and technique for its use in obtaining cytological material from the stomach are described.

2. The diagnostic value of the smear technique using the gastric balloon is evaluated in 238 cases with gastric diagnostic problems.

3. The possible relation of this diagnostic method to the early diagnosis of gastric cancer is discussed.

232 E. 66th St. (Dr. Cooper).

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**Occupational Eruptions.**—Occupational eruptions account for 60% of industrial disease, excluding actual accidents. For this reason great emphasis must be placed on proper screening of workers. . . . The physician should eliminate prospective employees with dermatoses which might be aggravated by the type of employment. . . . Workers with finely textured skin, as well as those with dry or senile skin, should not be employed where they contact strong primary irritants. Applicants who are light-sensitive (blondes and people with red hair and freckles) should not be hired in industries where they would contact petroleum products. . . . Individuals with atopic backgrounds, history of vasomotor instability (hyperidrosis and dysidrosis), are more likely to develop an eczematous dermatitis of the exposed parts, especially if they are going to do wet work. In some industries, individuals who do not perspire freely are to be preferred, while in other industries a moist skin may be of advantage. Workers having thick oily skin withstand the action of fat solvents such as soaps, turpentine, naphtha, benzol, and carbon tetrachloride better than those with dry skin. Persons with a history of former skin sensitization should be refused employment where the work would entail contact with known sensitizers. Atopic individuals, especially those with hand eczemas, prove to be particularly susceptible to dermatitis when exposed to wet work, cleansers, or irritants. Anyone with a severe chronic dermatophytosis should not be employed until he is free from eruption. It is thought by some observers that these individuals are more likely to develop a contact dermatitis, an "id" eruption, and subsequent eczematization. . . . Dark-skinned people are less affected by exposure to light, heat and petroleum products. Senile skin reacts poorly to wet work.—Harold G. Ravits, M.D., Occupational Aspects of Eczema, *Minnesota Medicine*, September, 1952.

# CARCINOMA OF STOMACH

## COMPARISON OF THREE SERIES OF SURGICAL CASES IN LARGE GENERAL HOSPITAL

*Frederick Fitzherbert Boyce, M.D., New Orleans*

In 1940, after a review of the world literature and an analysis of 14,000 gastrectomies for carcinoma of the stomach, Pack and Livingston,[1] whose vast personal clinical experience in this disease enabled them to speak with authority, set forth 65 conclusions. The first was that cancer of the stomach is a curable disease. The 19th was that if "every individual with gastric carcinoma received treatment in the type of surgical clinic which has furnished the most impressive rate of definitive cures, still 95 per cent or more of all afflicted would die of the disease within less than two years." The 20th was that for "approximately 75 per cent of patients with the disease surgery offers not the faintest hope for cure."

At the 1941 annual session of the American Medical Association, I presented before the Section on Surgery, General and Abdominal, a review of 200 surgical cases of carcinoma of the stomach treated at Charity Hospital of Louisiana at New Orleans.[2] It supplemented a similar survey published in 1933.[3] These present remarks, which concern the 200 most recent surgical cases treated at Charity Hospital, are based upon a continuation of those two previous analyses. All three analyses fully bear out what Pack and Livingston said more than 10 years ago about the deadliness of this disease. Unfortunately, even the latest analysis makes it only too clear that some patients with curable carcinoma, because of errors and omissions on the part of the profession itself, are not being given the chances of cure that they might otherwise have. The best results in this disease are bad. We cannot afford to make them worse than they already are. Yet that is exactly what some of our policies and practices amount to.

The background for these 600 surgical cases (fig. 1) is the more than 4,000 cases of carcinoma of the stomach treated at the hospital over the 30 year period ending in 1951. The third period shows a distinct improvement over the two earlier periods in that almost half of all the patients admitted with this disease were given whatever chance surgery might hold for them. That was true of little more than a third of the patients admitted during the first period and of considerably less than a third of those admitted during the second. The surgical mortality, which is the only mortality that really matters, has also shown a considerable improvement during this last period. It is a commentary upon the deadliness of gastric cancer that one should feel a certain unhappy satisfaction because in this last period, for the first time in these three decades, surgical deaths were more numerous than nonsurgical deaths.

### DISTRIBUTION OF OPERATIONS: SURGICAL MORTALITY

A comparison of the 200 surgical cases in each of the periods analyzed (fig. 2) shows that in the most recent series just over half of the operations were gastrectomies. This is an increase of 83.6% over the 1941 series and of 180.6% over the 1932 series. On the other hand, the actual facts are not as good as these figures might suggest. They do not mean that a larger number of patients who can be cured are being seen. The increase can be explained in three ways: (1) by a commendably bolder and more aggressive attack upon the disease, (2) by an extension of indications for resection, which was also commendable but was perhaps sometimes overgenerous, and (3) by the present general tendency to substitute gastrectomy for gastroenterostomy as a palliative operation.

Much of the encouragement that one might otherwise derive from the notable increase in resections in this last period is vitiated by the fact that only 43 of the 101 gastrectomies were undertaken with any idea that they might be curative. On the other hand, the results of palliative operations were not entirely discouraging. The immediate hospital mortality was lower than the mortality of gastroenterostomy. Many of the patients who lived for varying periods of time after operation had comfortable, and

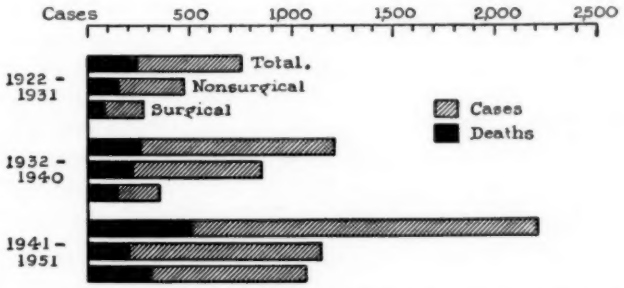


Fig. 1.—Distribution and mortality, surgical and nonsurgical, of 4,178 cases of carcinoma of stomach at Charity Hospital of Louisiana at New Orleans, 1922-1951.

sometimes active and useful, months or even years of survival. In many instances the span of life was longer. In terms of survival, in fact, the short-term results of the palliative operation compare favorably with those of curative gastrectomy. Of the 31 patients who survived presumably curative gastrectomy and who could be followed up, 15 are still alive from 4 to 27 months after operation. Of the 51 survivors followed up after palliative resections, 11 have lived from 4 to 25 months, and 3 others have survived 31, 35, and 36 months respectively and still regard themselves as well.

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Because of space limitations, some of the bibliographic references have been omitted from THE JOURNAL and will appear in the author's reprints.

Read before the Section on Surgery, General and Abdominal, at the 101st Annual Session of the American Medical Association, Chicago, June 12, 1952.

1. Pack, G. T., and Livingston, E. M.: Treatment of Cancer and Allied Diseases, New York, Paul B. Hoeber, Inc., 1940.

2. Boyce, F. F.: Carcinoma of the Stomach in a Large General Hospital: A Comparative Study of 2 Series of Surgical Cases from Charity Hospital of Louisiana at New Orleans, J. A. M. A. **117**: 1670-1675 (Nov. 15) 1941.

3. Maes, U.; Boyce, F. F., and McFetridge, E. M.: The Tragedy of Gastric Carcinoma: A Study of 200 Surgical Cases, Ann. Surg. **98**: 619-634 (Oct.) 1933.

Total gastrectomy, which appears for the first time in the 1952 analysis, was performed 11 times (in eight cases with the idea of cure). There were two hospital deaths. Of the eight survivors followed up, four died within 2 to 8 months after operation and two others at 12 and 21 months respectively. One is alive nine months after op-

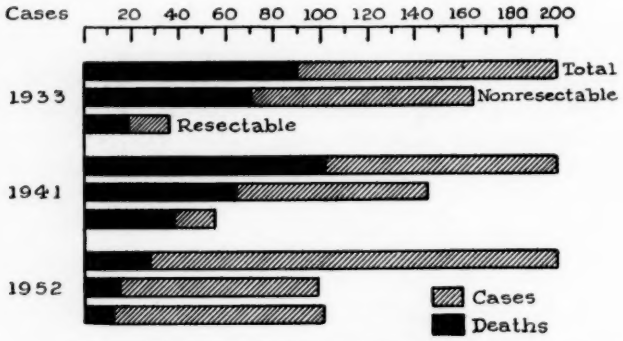


Fig. 2.—Comparative resectability and mortality in three series of surgical cases (200 each) of carcinoma of stomach.

eration, but his condition is apparently terminal. The remaining patient is still alive and in fairly good condition 35 months after total gastrectomy and 13 months after enteroenterostomy for a metastatic obstruction of the jejunum that could not be resected because its excision would have jeopardized the regional blood supply. The indications for total gastrectomy were clear-cut in all 11 patients; it was this operation or none at all. These cases, in fact, prove again that in this disease the stage and location of the growth, not the skill and ability of the surgeon, determine the end result for the individual patient. I doubt that total gastrectomy will ever have a wide field of usefulness in this particular hospital. As these

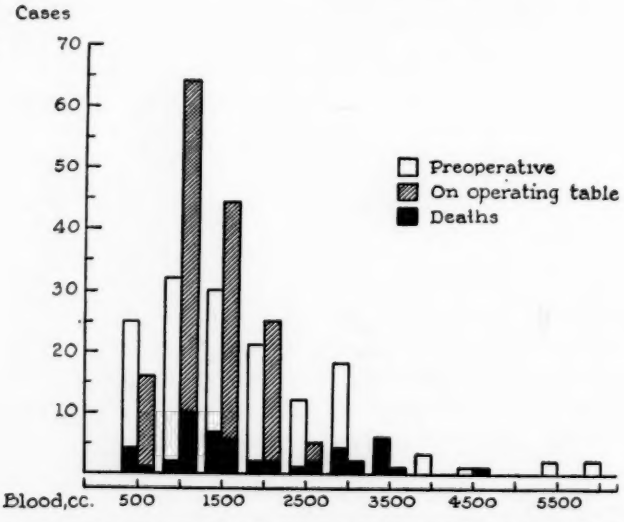


Fig. 3.—Use of whole blood before and during operation in 200 surgical cases of carcinoma of stomach (1952 series).

records show, patients who cannot receive the dietary care and compensatory therapy that loss of the stomach requires sometimes find the mere prolongation of life a heavy burden indeed.

The mortality in this third series of operations for carcinoma of the stomach, while still deplorably high, represents a considerable improvement over the two earlier series, particularly for gastrectomy (fig. 2). The improvement, in one sense, is less striking than the figures indicate: In numerous instances in the first series, and in a smaller number in the second, the patients who died after operation never left the hospital because there was nowhere else for them to receive terminal care. Now that welfare benefits and the provision of other facilities have altered this situation, it is the policy of the hospital, except in cases of extreme urgency and hardship, to keep its beds free for patients who can still be helped. There is, nonetheless, a real improvement in the mortality of the 1952 series, for which there are a number of explanations. One is the resident system now in effect at Charity Hospital. It did not exist when the first analysis was made, and it affected only a small number of the cases studied in 1941. Incidentally, while all 200 operations in the first series, and all but a few in the second 200, were performed by members of the hospital staff, three-quarters

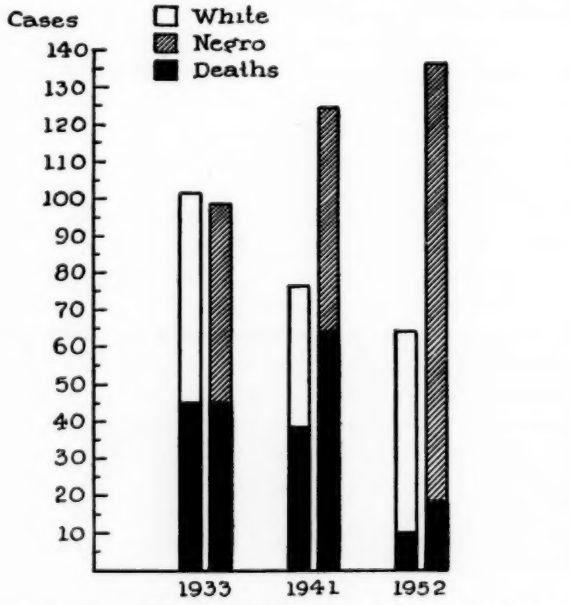


Fig. 4.—Comparative racial incidence and mortality in three series of surgical cases (200 each) of carcinoma of stomach.

of the operations in the last series were performed by resident physicians. The decrease in mortality is further proof of the safety of permitting properly trained and supervised younger men to undertake serious surgery.

Shock, hemorrhage, peritonitis, and pneumonia, which accounted for more than half of all deaths in the first series and for almost half in the second, have been almost eliminated as causes of death in the 1952 series. Antibiotic therapy, which was available only in the most recent series, played an important role in this elimination, but its value must not be overemphasized. Other factors were of equal or greater importance. Preoperative and postoperative care, chiefly as the result of the resident system just mentioned, was generally excellent; in fact, there were not more than five cases in the whole 200 in which it was open to criticism. It included careful stabilization of the fluid balance, judicious replacement of electrolytes, the use of protein hydrolysates, and constant intestinal decompression, particularly before operation. Anesthesia was far more competent in this series than it

was in either of the earlier two. Active measures were employed to prevent postoperative respiratory infections. Early ambulation was almost a routine practice. Probably most important of all these measures, however, was the liberal use of whole blood before operation, on the operating table, and after operation if it was still needed (fig. 3). In the 1933 series, transfusion was used only occasionally and, as a rule, only after severe hemorrhage or when a patient was dying. In 1941 a blood transfusion was still an event of consequence. In the years since then, transfusion for preparatory and prophylactic purposes has become a standard procedure and undoubtedly accounts for the major improvement in postoperative mortality evident in the 200 operations that have been done most recently.

The mortality of exploratory laparotomy was high in all three series, including the latest. The explanation is the usual one, that the operation was oftenest performed on patients who represented poor risks. Most of the deaths following laparotomy were the result of cachexia and inanition, which could not be overcome even by intensive adjunct therapy. If exploration were advanced to its proper status in carcinoma of the stomach, it would be used as a diagnostic tool, would be performed early in the disease in patients who still represented good risks, and would be undertaken with the hope and expectation that if the lesion proved to be malignant, exploration could become resection. Moynihan's aphorism, that surgical exploration for purposes of inquiry should carry no mortality with it, might then really become true.

Jejunostomy does not appear in the 1952 series as a primary procedure. It was performed 13 times in the first series and 7 times in the second, with a combined total of 18 hospital fatalities in the 20 cases. Gastrostomy was performed in six patients in the last series. If gastrostomy had not been performed, the patients would have starved to death. As it was, three of the six died in the hospital. Three secondary operations were done in the 1952 series in patients who had previously undergone subtotal gastrectomy. One was a resection of the stump of the stomach, one a gastroenterostomy to relieve obstructive symptoms, and the third merely an exploration. Three secondary operations were also done for obstruction. These secondary procedures, of course, in no way resemble the "second look" that Wangensteen [4] has been advocating. The plan has given excellent results in his hands, but I doubt that it will ever be widely applied in a large public hospital with a large Negro population.

I might say that in these three analyses the incidence of carcinoma of the stomach in Negroes has about paralleled the racial changes in the hospital population (fig. 4), which is now about 60% Negro. The white and Negro surgical mortality has been of about the same order, and in the most recent surgical series studied the proportion of gastrectomies in each race was also substantially the same.

## PRESENT STATUS OF DIAGNOSIS AND TREATMENT

In spite of the improvement evident in this last series of operations, a number of disturbing facts have emerged from the analysis. The number of gastrectomies performed each year since 1941, the date of the previous analysis, has been small; and it may be that the element of chance accounts for the unevenness of the mortality, which was higher in 1951 (fig. 5) than in several of the previous years. Other considerations, however, seem of real significance.

Time lag is a most important factor in mortality. Harvey and his associates,[5] in an analysis of a 34 year

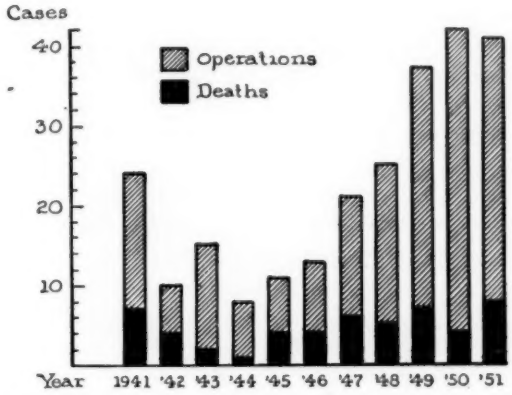


Fig. 5.—Yearly incidence and mortality for carcinoma of stomach, 1941-1951.

experience with carcinoma of the stomach at the Presbyterian Hospital in New York, were disturbed by the fact that the duration of symptoms before medical consultation was as long in the later years of the study as in the earlier years in spite of the increasing willingness of the surgical staff to operate on mere suspicion. Welch and Allen [6] commented on the same lack of improvement in two 10 year studies from Massachusetts General Hospital. If the curves for the two series were superimposed, they pointed out, they would almost exactly coincide. In the most recent series from the New Orleans Charity

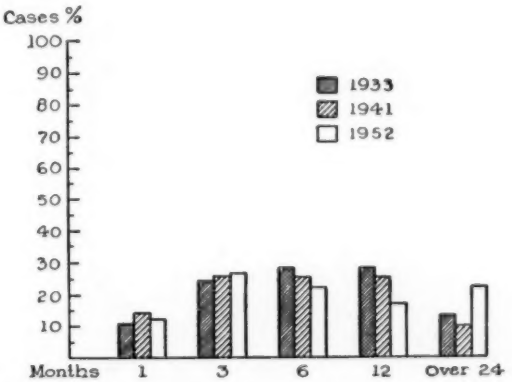


Fig. 6.—Time lag, in months, from onset of symptoms to hospitalization in three series of surgical cases (200 each) of carcinoma of stomach.

Hospital, the time lag is no more encouraging (fig. 6). The record of what Byrd,[7] who was discussing carcinoma in physicians, has well called "the fatal pause" is actually

4. Wangensteen, O. H.: Cancer of the Esophagus and the Stomach, New York, American Cancer Society, Inc., 1951.

5. Harvey, H. D.; Titherington, J. B.; Stout, A. P., and St. John, F. B.: Gastric Carcinoma: Experience from 1916 to 1949 and Present Concepts, Cancer **4**: 717-725 (July) 1951.

6. Welch, C. E., and Allen, A. W.: Carcinoma of the Stomach, New England J. Med. **238**: 583-589 (April 22) 1948.

7. Byrd, B. F., Jr.: Fatal Pause in Diagnosis of Neoplastic Disease in Physician-Patient, J. A. M. A. **147**: 1219-1220 (Nov. 24) 1951.

somewhat worse than in the earlier series. In the 1952 series, 82 patients waited more than six months to enter the hospital, and 33 others waited more than a year.

Harvey and his associates [5] also mention with regret "the culpability of the profession" in carcinoma of the stomach. Although many of their records did not mention previous care at all, they found that a majority of their patients had consulted physicians before half of the preadmission duration of symptoms had elapsed, and that in half of all cases the physician was responsible for a longer period of delay than was the patient. The Charity Hospital figures are to much the same effect. In all, 101 of these 200 patients consulted 129 private physicians before they applied to the hospital. Eight persons with resectable cancers and the same number with nonresectable growths were referred to the hospital at once, frequently with the correct diagnosis. Forty-three patients with resectable and 42 with nonresectable growths were treated medically outside of the hospital for periods ranging from two weeks to two years.

Nor was this the only delay. It might reasonably be expected, as Guiss [8] says, that the delay caused by a patient before he consults his physician, added to a second delay, the time required for diagnosis, would equal a third figure, the total time from the onset of symptoms to the institution of treatment. Nothing could be further from the truth. In his experience, which is borne out by the Charity Hospital experience, there is another period of delay before active treatment is instituted; that is, if the sum total of these delays does not make it too late to institute any treatment at all. Two or three weeks of hospitalization seem a fairly liberal allowance for the making of a diagnosis, if it has not been made before admission, and for the preparation of a patient for operation. At Charity Hospital, however, 58 of the 101 patients with resectable growths were in the hospital between 14 and 41 days before they were brought to the operating room. Of the 99 with nonresectable growths, 62 were in the hospital between 14 and 43 days before operation. In other words, only 40% of these 200 patients were operated on within two weeks of their admission to the hospital. Guiss [8] explains delay in diagnosis and treatment in carcinoma of the stomach on two grounds: first, the belief in many medical circles, not excluding the faculties of medical schools, that cancer of the stomach is hopeless from the onset, and second, an "unjustifiably optimistic rationalization" over the roentgenologic report. This present series provides at least six other explanations, which are discussed herewith.

1. Outside of the hospital, and sometimes in the clinics and wards as well, the tendency was to prescribe for the patient's symptoms without a serious attempt, if any attempt at all, to find out what caused them.

2. The ulcer-cancer problem rears its head again in this series, as it has in the two previous series of surgical cases studied at Charity Hospital (see footnotes 2 and 3) and in about the same proportion, i. e., almost a quarter of the cases. Twenty-four patients had a typical history of peptic ulcer, for which most of them had previously been treated. They may or may not have had benign lesions in the past. Nineteen other patients were treated on the same diagnosis by private physicians, and five more were treated in the hospital clinics in the course of their current illnesses. These facts simply prove again the utter impossibility of determining by clinical, roentgenologic, or any other means whether one is dealing with a benign or a malignant lesion. They also prove another of Moynihan's aphorisms, that one cause of death in carcinoma of the stomach is the successful medical treatment of the malignant lesion that masquerades as a benign ulcer.

This experience is not at all unusual. I have commented on it in my two previous studies of carcinoma of the stomach from the New Orleans Charity Hospital. Lampert, Waugh, and Dockerty [9] recently reported a 13% diagnostic error in 550 operations for presumably benign ulcers at the Mayo Clinic. Allen [10] puts the error for a 10 year period at Massachusetts General Hospital at 14%. At the Lahey Clinic it was almost 20%.[11] Up to 1945 the policy at the last-named institution was to subject patients with presumed gastric ulcers to a period of closely supervised medical treatment. The precautions employed, together with the superior qualifications of the gastroenterologists on the clinic staff, seemed to make this an eminently safe procedure. Now a month's trial of medical treatment is regarded as too long.

3. In addition to the mistaken treatment of cancers as ulcers, other patients in this series, usually outside of the hospital, were treated for a bewildering variety of other diseases, most of which they did not have. One was operated on for gallbladder disease, one for chronic appendicitis, two for umbilical hernia, and another for prostatic disease. Two patients were given penicillin, and one was also given a sulfonamide, for reasons that are not clear. Belladonna, however, occupied the disastrous position held by the antibiotics in the delayed diagnosis of carcinoma of the lung. Paregoric was sometimes prescribed also. Two patients were treated by 9 and 24 injections respectively, apparently for anemia. Most of these patients seem to have been treated in this manner because carcinoma of the stomach was not suspected or because, if it was, the investigation was perfunctory and negative findings were accepted without question. The patients, of course, treated themselves with the variety of patent medicines advertised over the radio for acid indigestion, as well as with such panaceas as "hadacol," the allurements of which quite canceled out the less attractive warnings of the American Cancer Society and similar organizations.

4. This series of cases, like all similar series, represents many missed opportunities. Some patients had been registered in the clinic for years and were under treatment for hypertension, cardiac disease, dermatological and orthopedic conditions, and other passing or chronic illnesses. Several were operated on for cataracts. In

8. Guiss, L. W.: Collective Review: End Results for Gastric Cancer: 2,891 Cases, Internat. Abstr. Surg., in Surg., Gynec. & Obst. **93**: 313-331 (Oct.) 1951.

9. Lampert, E. G.; Waugh, J. M., and Dockerty, M. B.: The Incidence of Malignancy in Gastric Ulcers Believed Preoperatively to be Benign, Surg., Gynec. & Obst. **91**: 673-679 (Dec.) 1950.

10. Allen, A. W.: Significance of Gastric Ulcer and Cancer of the Stomach, Rhode Island M. J. **34**: 425-427; 431 (Aug.) 1951.

11. Marshall, S. F., and Welch, M. L.: Results of Surgical Treatment for Gastric Ulcer, J. A. M. A. **136**: 748-752 (March 13) 1948.

all these cases the gastric carcinoma seems to have developed while the patients were under direct medical observation for disease in some other area of the body.

5. A frankly alarming fact is evident for the first time in this most recent series of surgical cases of carcinoma of the stomach, what Andresen [12] calls "the present day disastrous emphasis upon psychosomatic medicine." It was indeed disastrous in some instances. Shorter [13] has also commented on it. The psychiatrist, he says, can always find some sort of psychic trauma to explain symptoms, though it should be said in his defense that when he receives a patient in consultation he has a right to assume that all possibilities of organic disease have already been exhausted. Some of the Charity Hospital patients were treated for their "nerves" before they applied to the hospital. In one instance there was no direct contact between physician and patient; his wife simply telephoned a description of his symptoms, and the druggist filled the prescription that was telephoned to him. Seven patients admitted to the clinics or wards had more active neuropsychiatric treatment. Two were thought to have ulcers with large functional overlays. Three were regarded as frankly neurotic, though in one of these cases the possibility of the male climacteric was also introduced.

Two cases deserve a more extended comment. One patient, after his gastrointestinal roentgenograms were reported negative, moved back and forth between medical and neurological clinics for five months, obstinately declining, as the resident physician petulantly noted, "to accept any ray of insight into his condition." The comment is illuminating. So is the fact that the patient's one idea, according to the consultant, was to give up his job and "go on relief," while it was the physician's equally passionate determination that this man, at least, should not be added to the relief rolls. Another patient, with a presumed gastric ulcer, confirmed by gastroscopy, was treated on and off for seven months before surgical consultation was requested. His recurrent symptoms, according to the student recorder, were chiefly caused by resentment, partly against his wife of 23 years and partly against his brother-in-law. His resentment, wrote the student in all seriousness, was so suppressed that it would be dangerous to inquire further into his emotional health. It was extremely dangerous not to inquire further into his gastric status and that of the other patients in this group. Delay in these cases ranged from two to seven months. Two of the seven patients, when finally operated on, had inoperable growths. The other five were subjected to palliative resection. I am not intending to imply that in all of these cases, if, indeed, in any of them, the period of delay for neuropsychiatric consultation and treatment was responsible for the findings at operation. I am disturbed by this new trend, however, and frankly alarmed by its popularity with medical students, interns, and resident physicians.

6. Investigation was perfunctory in some of these 200 cases. In most of them, on the contrary, it was almost too detailed and repetitious. Diagnostic studies were repeated, sometimes more than once, even when the first reports were conclusive or pointed so strongly to malignant disease that immediate exploration seemed warranted. Often the reason for the delay was not clear: reluctance to accept a diagnosis of gastric carcinoma, perhaps, or a desire to make an incontrovertible preoperative diagnosis, or an unwillingness to accept the results of any single diagnostic test. For my own part, if clinical observation and roentgenologic examination point to carcinoma of the stomach, I can see no reason for doing anything more than prepare the patient for exploratory laparotomy. The suspicion may be unworthy, but I wonder whether the elaborate diagnostic routine, the repeated studies of hepatic and renal function, the hemograms, and other tests were not ordered, at least in some cases, simply because of the ease with which multiple studies can be made in a public hospital. I also have the suspicion, perhaps equally unworthy, that sometimes little more was done with the reports than to attach them to the chart.

## PRESENT SOLUTION OF PROBLEM

The solution of the problem of carcinoma of the stomach obviously lies in case finding or, more correctly, in the finding of early cases. No method so far tried has proved successful. Routine roentgenologic methods are impractical for general use, even when they are carried out selectively.[14] Their selective use, in fact, requires preliminary screening, which, while it slightly improves the meager results, adds to the expense and the cumbersomeness of the method. Photofluorography, as employed at the Johns Hopkins Hospital,[15] has identified some cases of gastric cancer but not the early, operable cases for which the project was set up.

My own, admittedly pessimistic, opinion is that we shall remain about where we are in the detection of early, silent carcinoma of the stomach until some serologic test is devised that will do for latent malignant disease of the internal organs what the Wassermann test has done for syphilis. Ivy,[16] among others, has pointed out the potential importance of this line of investigation. I should like to see far more attention devoted to this objective in current research programs, even if it means slighting, at least for the present, other worthy objectives. After all, unless the diagnosis is made, and made relatively early, no technical or other skill will avail the patient with carcinoma of the stomach. I might add that whatever screening test is eventually devised will have to be simple, painless, and quickly performed. People wish to be saved, but they demand that their salvation be accomplished without inconvenience or discomfort.

In the meantime, I recommend that the profession take stock of its teaching methods. Charity Hospital in New Orleans is a teaching institution. Its intern and resident staff is composed of graduates of many medical schools in all parts of the country. Many of these young physicians have apparently not been taught that diagnosis in carcinoma of the stomach is a matter of extreme urgency and that, to quote Moynihan again, the certainty of diagnosis may also be the certainty of death. That point must be stressed, in season and out, in professional teaching.

12. Andresen, A. F. R.: The Problem of Gastric Cancer, New York J. Med. 51: 2115-2122 (Sept. 15) 1951.

In this disease, nothing equals in value a well taken clinical history, beginning with the first departure from health that the patient can recall and continuing chronologically to the time of his hospital admission. Laboratory aids, useful as they are in their proper place, are of no value at all unless they are correlated with clinical observations. One is almost tempted to require for medical students, interns, and resident physicians daily periods of reflection and meditation upon the case histories and laboratory reports of all their patients, with carcinoma of the stomach in mind. Certainly there is needed far more of the vigor exhibited—I find this extremely hopeful—by a fourth year medical student who was assigned to a case in which investigation was proceeding at a leisurely pace and gastric carcinoma had not yet been considered. He wrote on his progress notes, "I say this man has cancer of the stomach and I'll have to be shown that he doesn't!"

Pack and McNeer [17] were eternally right when they wrote that the management of carcinoma of the stomach is a philosophy quite as much as a technique. A surgeon, they said, has no right to treat the disease at all if his philosophy does not urge him to attempt the removal of every gastric cancer that he encounters. That statement of principle should be extended to include the medical man who first sees the patient, and who also has no right to treat him if he does not intend to expedite both diagnosis and surgical consultation.

One of the most disturbing things about this analysis is that it shows the continuing need to say again things that were said definitively many years ago. In 1900 the late W. J. Mayo [18] wrote, "The scientific zeal with which diagnosis is sought has in itself a distinct danger." The sensible practitioner, he continued, with a few simple means at his command is perfectly capable of arriving at a diagnosis in this disease. In that same paper he said, "The exploratory incision for suspected cancer of the stomach, instead of being a last resort, should be one of the first, and promptly undertaken if the condition cannot be proved to be nonmalignant." In 1903 he went back to the same themes [19]: "The hope for the future lies in early exploratory incision, and the necessity for this depends upon clinical observation rather than laboratory methods, which too often only become valuable when the extent of the disease is beyond cure. . . . When we consider that early operation is the only hope, we may not wait on our own responsibility." In 1905 he summed up the whole matter even more bluntly [20]: "Now I do not think a medical man has any more business to have a case of cancer of the stomach in his ward than he has to have a case of cancer of the lip, for the reason that cancer of the stomach is not a medical disease—it is purely surgical." The late W. H. Welch [21] had summed up the matter equally well 20 years earlier: "The opinion entertained by the physician as to the propriety of surgical interference in gastric cancer is not . . . a matter of indifference, for cases of gastric cancer come first into the hands of the physician, and generally only by his recommendation into those of the surgeon."

The observations of these dead and gone master physicians are as valid today as they were 50 years and more ago. In season and out we must teach them to our medical students, to the young surgeons for whose training we are responsible, and, as far as we can, to our medical confrères. If all of us put them into practice, it would do much, even in the present state of our knowledge, to alter the outlook in what Welch well termed the "relentlessly fatal forecast" of carcinoma of the stomach.

SUMMARY

The 200 most recent surgical cases of carcinoma of the stomach at Charity Hospital of Louisiana at New Orleans represent a considerable improvement over similar series studied in 1941 and in 1933. Gastrectomy was performed far more frequently, and the total surgical mortality, as well as the mortality for resection, was considerably lower than in the earlier series. Nonetheless, patients are still seeking treatment late. Physicians are still treating them symptomatically rather than investigating the cause of their symptoms. Gastric carcinoma is still being treated on the mistaken diagnosis of benign ulcer, although there is no positive clinical, roentgenologic, or other method of differentiating the one from the other. Negative laboratory reports are still readily accepted, while opposed to the lack of clinical suspicion of the disease is a tendency toward repetition of laboratory studies and delay in diagnosis, with a consequent delay in the institution of treatment. An alarming tendency was noted in this most recent analysis, i. e., the invocation of psychosomatic medicine to explain symptoms and signs caused by gastric cancer. The solution of the problem, in the light of present knowledge, is (1) more vigor in the prosecution of the diagnostic routine, and (2) a prompter and far more general resort to exploratory laparotomy in doubtful cases. There is nothing new about this program, but it has never been fully tried.

1413 Richards Bldg. (12).

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**Spiral Nature of Intestinal Musculature.**—It is not often that a fundamental discovery in the scientific world is overlooked for a considerable length of time and still less often does it happen that the same "discovery" should be made anew after a lapse of two hundred and fifty years. This, however, actually occurred in the case of the discovery of the spiral arrangement of the musculature of the intestines. It was on May 22, 1676, that the following paper was published in the Philosophical Transactions of the Royal Society: "A discourse concerning the Spiral, instead of the supposed Annular, structure of the Fibres of the Intestins; discover'd and shewn by the Learn'd and Inquisitive Dr. William Cole to the R Society." . . . Dr. Cole did not, at first, take any steps to find any anatomical proof of this conjecture, but eventually, considering that "t'was too unphilosophical to acquiesce in bare speculation, when autopsy might be consulted," he decided to make some experiments. He first investigated the intestines of an Ox, "which, by reason of their largeness of proportion to those of most other species of animals, seem'd fittest for the tryal; afterwards in those of Sheep and Calves, beside the repetition of it in Oxen, and not only in the smaller intestines, but in the colon and caecum also." . . . This observation was entirely overlooked and the stereotyped description of longitudinal and circular layers of intestinal musculature persists in textbooks until this day. It was not until 1921 that Dr. Eben J. Carey's paper in the Anatomical Record entitled "Studies on the structure and function of the small intestine," completely confirmed the correctness of Cole's observations which, however, were quite unknown to Carey.—J. Dobson, M.D., *Proceedings of Royal Society of Medicine*, July, 1952.

# EFFECT OF PROGRESSIVELY BUFFERED SOLUTION OF EPHEDRINE ON NASAL MUCOSA

*Noah D. Fabricant, M.D., Chicago*

Nasal vasoconstrictors occupy a commanding position among the various therapeutic measures employed by the general public for relief of nasal congestion and the common cold. Ephedrine, the first nasal vasoconstrictor to be introduced into clinical practice, is still the most widely used. Its success has led to the synthesis of other nasal vasoconstrictors, some more potent, others less potent, than ephedrine. Although ensuing relief is temporary, overcoming the discomfiture caused by intranasal obstruction is welcome to distraught patients. There is little to indicate that the current passion for psychosomatic phraseology will alleviate millions of inflamed and allergic American noses.

For physicians to disregard the opportunity of palliation, when such effect is easily possible, is tantamount to complete therapeutic neglect. Since the function of physicians is to prescribe measures of relief in the event a cure cannot be obtained, habitual rejection of the use of so simple a therapeutic device as a physiological nasal vasoconstrictor in the treatment of intranasal congestion will often drive patients to over-the-counter purchases and self-medication.

The creation of standards for rational nasal medication has been assisted greatly by cognizance of the histological and physiological effect of various nasal preparations on nasal or sinal mucous membrane, ciliary motility, and the hydrogen ion concentration of nasal secretion, and by noting the presence or absence of local and systemic side-effects. Fantus' [1] dictum that a hydrogen ion concentration near that normal to the mucous membrane is more important in solutions for application to the mucous membranes than the isotonicity has provided a firm foundation for rational physiological nasal medication. So far as concerns the pH values of local medicaments, valid therapeutic conclusions have been drawn in a variety of clinical fields from measurements of the hydrogen ion levels of various secretions found in their original positions on underlying mucous membrane and tissue surfaces.

During the past decade, several communications have appeared calling attention to the local effect of nasal medicaments with various pH values on the nasal mucous membranes of laboratory animals and human subjects. At a time when the introduction of the local use of sulfonamide compounds as prophylactic and curative agents in the treatment of infections of the nasal cavity and paranasal sinuses was being greeted with unrestrained zeal, a note of disillusionment was struck by Fletcher,[2] who reported necrosis and charring of the mucous membranes of the maxillary sinus following irrigation of the sinus with highly alkaline 5% and 10% solutions of sodium sulfathiazole over a three week period. Futch [3] and his associates observed the effect of 5% and 10% solutions of sodium sulfathiazole with an approximate pH of 10 on the nasal mucous membranes of rabbits, and found that 5% solution of sulfathiazole sesquihydrate exerted an early and destructive effect on the nasal mucous membrane. Hunnicutt [4] instilled 0.5%, 1%, and 5% solutions of sodium sulfathiazole in the nasal cavities of mice three times a day for 14 days. Purulent exudate was detected during the first three days in about half the mice. Gundrum [5] studied the effect of 4.7% solutions of sodium sulfathiazole, sodium sulfadiazine, and butanoylsulfanilamide on the nasal mucous membranes of rabbits. Microscopic study of the nasal tissues of the animals treated with sulfanilamide derivatives showed injury to the entire nasal mucous membrane, with great damage to the olfactory area. This was more pronounced in animals in which sodium sulfathiazole and butanoylsulfanilamide were used. Sodium sulfadiazine, while not so completely destructive, was definitely injurious. Dickson tested six commercial sulfonamide nasal preparations on the nasal mucous membranes of rabbits and found no injury produced by preparations with pH values ranging from 5.0 to 9.4.

Callomon [6] studied the microscopic tissue changes produced in the nasal mucous membrane of normal mice by prolonged local administration of various sulfonamide compounds with different pH values. In varying degree, tissue changes were found during treatment with all the sulfonamide compounds, with pronounced differences of degree in the injury instituted by the preparations. The least irritation was noted in animals given a 3% solution of sulfathiazole in propylene glycol (pH 5.1), with a pH value near the normal physiological range of nasal secretions in man. The greatest injury and a slow return to normal were observed following use of 2% solution of sulfoxone (diasone®) in propylene glycol, which evinced the highest acidity among the solutions used (pH 4.8). One of the commercial preparations, a combination of desoxyephedrine and sodium sulfathiazole in aqueous solution (pH 9.2), caused an inflammatory and partly caustic effect. Finally, Hollender, Anderson, and I conducted studies on rabbits demonstrating that various solutions of sodium and calcium penicillin (containing from 1,000 to 5,000 units per cubic centimeter) applied topic-

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From the Department of Pathology, Mount Sinai Hospital and Mount Sinai Medical Research Foundation.

Dr. Kurt Stern, Assistant Director, Mount Sinai Medical Research Foundation, assisted in the histological study made in preparing this paper.

1. Fantus, B.: General Technic of Medication, ed. 3, Chicago, American Medical Association, 1938.

2. Fletcher, R.: Sodium Sulfathiazole: Its Caustic Reaction, Calif. & West. Med. **55**:94, 1941.

3. Futch, C. E.; Rosenvold, L. K., and Stewart, C. E.: Caustic Effect of Sodium Sulfathiazole Solution on Nasal Mucous Membranes: Results of Animal Studies, J. A. M. A. **119**:7 (May 2) 1942.

4. Hunnicutt, L. G.: Reaction of Mucous Membranes to 5 per cent Solution of Sodium Sulfathiazole, Arch. Otolaryng. **36**:837 (Dec.) 1942.

5. Gundrum, L. K.: Effect of Newer Sulfanilamide Derivatives on Nasal Mucosa of Rabbits: Preliminary Report, Arch. Otolaryng. **37**:209 (Feb.) 1943.

6. Callomon, F. T.: Tissue Changes Produced in the Nasal Mucous Membrane of Normal Mice by Prolonged Local Administration of Some Solutions Containing Sulfonamide Compounds, Arch. Otolaryng. **43**:31 (Jan.) 1946.

ally to the respiratory nasal mucous membrane of rabbits for prolonged periods have no deleterious effects. The pH of the solutions employed ranged from 6.0 to 6.5.

## METHOD OF STUDY

In this study a single nasal vasoconstrictor preparation was employed; an attempt was made to have all components alike except for progressively buffered differences in pH values. In investigations undertaken by others, it should be pointed out that the various nasal preparations used differed not only in pH values but in chemical structure as well. This introduced elements into the study that made difficult a proper evaluation of the pH factor in nasal medication.

Forty-five rabbits were employed in the present investigation, of which five died during the course of experimentation. The right nasal passages of 40 presumably normal rabbits received a progressively buffered solution of 1% ephedrine hydrochloride in isotonic sodium chloride solution; the left nasal passages served as controls. The pH range of the appropriate nasal solutions were prepared according to the following phosphate systems:

| Phosphate Systems | pH Range |
|---|---|
| $KH_2PO_4$ $H_3PO_4$ | 2.5 — 5.0 |
| $KH_2PO_4$ $Na_2HPO_4$ | 5.2 — 8.0 |
| $Na_2HPO_4$ NaOH | 8.0 — 12.0 |

Each of the treated animals received three drops of the appropriately buffered isotonic nasal solution from a standard medicine dropper three times daily for 30 days. Two rabbits received the 1% solution of ephedrine hydrochloride with each pH value, which was increased by increments of 0.5 in a range from pH 2.5 to pH 12. Thus two rabbits received a solution with a pH of 2.5, two a solution with a pH of 3.0, two a solution with a pH of 3.5, two a solution with a pH of 4.0, etc.

Each of the animals was killed at the end of 30 days by means of an intravenous injection of air. After the turbinal structures were removed, sections were prepared for histological study. Hematoxylin and eosin stains were used.

## RESULTS

At autopsy, the treated nasal cavities of nine rabbits contained varying amounts of gross purulent exudate, while the untreated nasal cavity of one rabbit evinced gross purulent exudate. In the former group, gross purulent exudate was demonstrated in animals treated with solutions of 1% ephedrine hydrochloride buffered to pH 3.0, 3.5, 4.0, 4.5, 7.0 (in both rabbits), 11.5 and 12.0 (in both rabbits). The single rabbit whose untreated nasal cavity showed gross purulent exudate was the one whose treated nasal cavity had received the ephedrine preparation buffered to pH 4.0.

In numerous instances the microscopic sections revealed a similarity between the ephedrine-treated and the untreated nasal mucous membranes, with minimal histological changes. For the most part, the pathological changes in the respiratory nasal mucous membranes consisted of slight to considerable hyperemia; acute, subacute, and chronic inflammation; and varying degrees of suppuration. The treated respiratory nasal mucous membrane of 13 of the 40 rabbits showed slight to considerable hyperemia, with the tissue of 3 displaying additional chronic inflammatory changes and suppurative foci. Varying degrees of acute and subacute inflammation and edema only were detected in 7 rabbits; acute and subacute inflammation with suppuration in 3 rabbits; acute and chronic inflammation in 2 rabbits; acute and chronic inflammation with suppuration in 3 rabbits; chronic inflammation only in 10 rabbits; and chronic inflammation with suppuration in 2 rabbits.

No appreciable histological changes were detected in the untreated nasal cavities of 8 animals, while slight to moderate hyperemia only was observed in 14 rabbits, and varying degrees of acute and subacute inflammation was found in 4 rabbits. In the remaining 14 rabbits, slight to moderate chronic inflammation occurred, with one of the animals showing suppuration.

## COMMENT

In a general way, this study reveals that the nasal mucous membrane of untreated nasal cavities of rabbits is less susceptible to histological change than the mucous membrane of nasal cavities that has been treated for 30 days with a progressively buffered solution of 1% ephedrine hydrochloride in isotonic sodium chloride solution. Highly acid solutions of 1% ephedrine hydrochloride (pH 3.0, 3.5, 4.0, and 4.5) and highly alkaline solutions of 1% ephedrine hydrochloride (pH 11.5 and 12.0) are more likely to produce traumatic and suppurative mucosal changes than either slightly acid or slightly alkaline preparations. Strangely, the two rabbits subjected to treatment with the nasal preparation buffered to a neutral pH 7.0 both evinced acute inflammation with gross purulent exudate in the treated nasal cavities. Just why this occurred is difficult to explain.

In considering the widespread use of laboratory animals in experimentation involving nasal administration of drugs, Kelemen and Sargent [7] point out that spontaneous pathological changes are not always fully appreciated. Such changes duplicate a large variety of conditions, ranging from slight inflammation to the most severe destruction, and are often claimed to be produced experimentally. This is true of both rats and rabbits. While studying the incidence of spontaneous sinusitis in rabbits, Hilding [8] observed infected paranasal sinuses in otherwise apparently healthy animals; he found that when a rabbit becomes ill or debilitated, rhinitis and sinusitis tend to develop. From these observations it may be concluded that the frequency of nonexperimental pathological changes warrants the utmost caution in evaluating findings that have been made by comparisons with conditions in "control" tissues or animals.

As for the nasal mucous membrane of the human nasal cavity, this structure is continuously subjected to the lashings of acute nasal infections, weather conditions, allergens, smoke, dust, and chemical substances. "Normal"

7. Kelemen, G. and Sargent, F.: Nonexperimental Pathologic Nasal Findings in Laboratory Rats, Arch. Otolaryng. 44: 24 (July) 1946.
8. Hilding, A. C.: Experimental Sinus Surgery: Effects of Operative Windows on Normal Sinuses, Ann. Otol., Rhin. & Laryng. 50: 379 (June) 1941.

respiratory mucous membrane, in the true sense of the term, exists only during the first few months of life, seldom remaining normal because of its vulnerability to inflammatory changes. Consequently, if inhalation of air produces changes in the respiratory mucous membrane of the human nasal cavity, it can come as no surprise that prolonged use of some nasal medicaments produces similar findings in one degree or another at the same site. In this connection, it may be inferred that the nasal mucous membrane of rabbits responds to its respiratory environment in like fashion; hence the occurrence in the present investigation of numerous instances of identical, minimal inflammatory changes in both the ephedrine-treated and the untreated nasal mucous membranes of the rabbit.

A laboratory animal such as the rabbit can generally be considered an important means for evaluating the local effect of nasal preparations on nasal tissues, since it is presumed to possess a mucosa more nearly comparable to that of human beings than the mucosa of any other laboratory animal. Nevertheless, there are occasions when the evidence and the conclusions derived from animal experiments—in this instance, the nasal cavity of the experimental rabbit—are limited in their applicability to the study and treatment of disease in man. Under such circumstances, further evidence should be sought in the human being himself.

### pH FACTOR IN HUMAN NASAL PHYSIOLOGY AND BACTERIOLOGY

Disturbances in the human nasal cavity are often an expression of altered physiological activity rather than the end result of gross pathological change. In this connection, one of the more important chemical phenomena involving nasal secretions is the pH, or the hydrogen ion concentration. Under normal conditions the secretions of the nose and the paranasal sinuses maintain a biochemical composition that fluctuates within a limited range according to the demands of physiological function, while under abnormal or pathological conditions the biochemical reactions are altered.

The pH of nasal secretion in situ in clinically normal adult nasal passages ranges from approximately 5.5 to 6.5, whereas in infants and young children it ranges from 5.0 to 6.7. During acute rhinitis, acute sinusitis, and the more active phases of allergic rhinitis, the pH of nasal secretion is found to be on the alkaline side, and then shifts back to the acid side when the stage of clinical resolution is reached.[9] Nasal pH varies with rest and sleep; prolonged rest and sleep promote an acid trend. Nasal pH is more acid during the night than during the day.

The relationship of the hydrogen ion concentration of nasal secretion to cellular reactions has been commented on independently by Tweedie [10] and Buhrmester,[11] who found that patients with pH values of 6.5 or below always had negative cultures. Tweedie made the observation that with elevation of the pH to the alkaline side, bacteria were usually found. Similarly, Buhrmester declared that all of her patients with a pH of 6.5 or below always had negative cultures. Both investigators expressed the belief that acidity as reflected in low values of pH is unfavorable to the growth of pathogenic bacteria, thereby furnishing evidence for the concept that nasal secretion in situ possesses a purposeful acid barrier against infection. Moreover, the work of Hansel demonstrates that in allergy it is especially significant that when the pH of nasal and sinal secretions falls low on the acid side, there is a complete disappearance of eosinophils, and when the pH returns to the alkaline side, there is a return of eosinophils. His investigation furnishes additional evidence that in recession from allergic attacks nasal secretion possesses a purposeful acid composition.

An important but imperfectly understood agent present in nasal secretions is lysozyme, a substance found in various body tissues and secretions that has the property of dissolving certain bacteria. Although lysozyme is most active against nonpathogenic organisms, it can attack pathogenic organisms when allowed to act in the full strength in which it occurs in some parts of the body. Fleming demonstrated that lysozyme preparations not only dissolve susceptible organisms but also kill them and inhibit their growth.

The action of lysozyme is influenced by hydrogen ion concentration, its activity being optimal at an acid pH. According to Hilding,[12] a sharp reduction of the lysozyme content of nasal mucus, with a consequent decrease in the antiseptic properties of nasal secretions, occurs during and preceding the invasive stages of the common cold (acute rhinitis). In some instances an increase in the lysozyme content of the secretion takes place on the same day as the beginning of subjective improvement. Since the action of lysozyme is known to be optimal at an acid pH, this may possibly explain why lysozyme is most active in the slightly acid nasal secretions of the clinically normal nose and why it is sharply reduced in the alkaline nasal secretions accompanying the acute common cold.

Hyperventilation is so common that its significance is frequently overlooked. Every person at some time finds himself in a state of hyperventilation. Chemical reactions of the body are quickly altered by changes in the concentration of the carbon dioxide in alveolar air. Loss of the carbon dioxide of alveolar air produces alkalosis within the body. Alkalosis may be induced voluntarily by deep and excessively rapid respiration. Alkalosis occasionally occurs during hysterical attacks as a result of hyperventilation (blowing off of carbon dioxide).

Alkalosis due to hyperventilation has been observed in persons suffering from neurologic disorders, anxiety neuroses, and hysteria. Hyperventilation frequently accompanies rage, sorrow, fatigue, excitement, and apprehension. The effort of crying seems to be made easier by hyperventilation. Just as emotional changes can cause vasomotor changes in the nasal mucosa of some noses, so they can convert for short periods nasal pH from a normal, slightly acid state to an abnormal alkaline state. Recently, children were instructed to blow 40 times against a sheet of tissue paper so that it would sway each

9. Fabricant, N. D.: Modern Medication of Ear, Nose and Throat, New York, Grune and Stratton, 1951.
10. Tweedie, A. R.: Reaction of Nasal Mucus, Acta oto-laryng. **24**: 151, 1936.
11. Buhrmester, C. C.: A Study of the Hydrogen Ion Concentration, Nitrogen Content and Viscosity of Nasal Secretions, Ann. Otol., Rhin. & Laryng. **42**: 1041 (Dec.) 1933.
12. Hilding, A.: Changes in the Lysozyme Content of the Nasal Mucus During Colds, Arch. Otolaryng. **20**: 28 (July) 1934.

time in response to the blowing off of carbon dioxide. Nasal pH readings were taken immediately before hyperventilation and immediately after the termination of the procedure. An alkaline nasal state ensued in many of the children and in most of those who cried.

Hyperventilation may also occur because of the increased respiratory rate associated with an increase in body temperature. It tends to take place in inflammatory conditions involving the respiratory passages, especially in pneumonia, and presumably can explain in part the reason for the alkaline nasal pH occurring during acute rhinitis, acute sinusitis, and the more active stages of allergic rhinitis. It is during the time of acute nasal embarrassment that the nasal mucous membranes are inflamed or congested, the secretions are increased, and nasal breathing itself becomes more labored. Hence nasal alkalosis takes place in response to the act of hyperventilation (blowing off of carbon dioxide). The return to a normal nasal acid state ensues when hyperventilation no longer occurs and clinical nasal improvement follows.

### pH FACTOR IN APPLIED CLINICAL PRACTICE

In recent years attempts have been made to direct the interest of rhinologists to the relation of the pH of nasal secretion in situ to applied nasal physiology, and to the importance of the pH factor in the field of nasal medication and applied clinical practice. Intranasal treatment by means of rational, physiological nasal medication requires not only treatment of mucous membrane surfaces (including ciliary action) but also treatment of nasal secretions (including the mucous blanket). Normal nasal secretion, including the mucous blanket, possesses a purposeful acid barrier against infection, for it has been observed that acidity as reflected in low pH values is unfavorable to the growth of pathogenic bacteria, and that nasal secretion possesses an acid composition when receding after allergic attacks.

I have conducted a lengthy series of experiments to determine the effect of a number of commonly employed nasal vasoconstrictors, topical anesthetics, silver preparations, and antiseptics on nasal pH. The pH of the nasal vasoconstrictors varied markedly from a highly acid 2.3 to an alkaline 9.5. I have discovered that the manner in which the trend of the nasal pH variation is affected depends of the pH of the drug employed. Thus, drugs with a highly alkaline pH induce in the nasal pH variation a pronounced drift toward alkalinity. Drugs with a pH range of 5.5 to 6.5 (as in the case of an appropriately buffered solution of 1% ephedrine hydrochloride in isotonic sodium chloride solution), which approximate the normal range of nasal pH, do not markedly affect nasal pH. Drugs with a pH level of less than 5 induce a drift downward in nasal pH, i. e., toward acidity.

Nasal vasoconstrictors possessing an unusually high alkaline pH value disturb the normal nasal pH level present in clinically normal nasal passages, enhance irritation of the nasal mucous membrane, and postpone the return of the nasal mucosa from a pathological alkaline status to a normal, slightly acid status. During an attack of acute rhinitis, acute sinusitis, and the more active stages of allergic rhinitis, the employment of a nasal vasoconstrictor that lowers the abnormal alkaline pH in these conditions to a normal, slightly acid pH level between 5.5 and 6.5 in adults or 5.0 and 6.7 in infants and children—in short, a physiological nasal pH—is most desirable in applied clinical practice.

### SUMMARY AND CONCLUSIONS

Nasal vasoconstrictors occupy a commanding position among the various therapeutic measures employed by the general public for the relief of nasal congestion and the common cold. Although ensuing relief is temporary, overcoming the discomfiture caused by intranasal obstruction is welcome to distraught patients. There is little to indicate that the current passion for psychosomatic phraseology will alleviate millions of inflamed and allergic American noses. For physicians to disregard the opportunity of producing palliation, when such effect is easily possible, is tantamount to complete therapeutic neglect. Since the function of physicians is to prescribe measures of relief in the event a cure cannot be obtained, habitual rejection of the use of so simple a therapeutic device as a physiological nasal vasoconstrictor in the treatment of intranasal congestion will often drive patients to over-the-counter purchases and self-medication.

In this investigation, the right nasal passages of 40 rabbits received measured instillations of a progressively buffered solution of 1% ephedrine hydrochloride in isotonic sodium chloride solution, the left nasal passages serving as a control, three times daily for a period of 30 days. The ephedrine preparation bore pH values ranging from 2.5 to 12.0. Each of the animals was killed at the end of 30 days, the turbinal structures removed, and sections prepared for histological study.

At autopsy, gross purulent exudate was demonstrated in animals treated with solutions of ephedrine buffered to pH 3.0, 3.5, 4.0, 4.5, 7.0, 11.5, and 12.0. In numerous instances the microscopic sections revealed a similarity between the ephedrine-treated and the untreated nasal mucous membranes, with minimal histological changes. For the most part, the pathological changes in the respiratory nasal mucous membranes consisted of slight to considerable hyperemia; acute, subacute, and chronic inflammation; and varying degrees of suppuration. Although in this study neutral solutions of ephedrine produced inflammatory reactions, in general highly acid and highly alkaline solutions are more likely to produce traumatic and suppurative nasal mucosa changes.

In the human nasal cavity, the pH of nasal secretion in situ in clinically normal adult nasal passages ranges from approximately 5.5 to 6.5, whereas in infants and young children it ranges from 5.0 to 6.7. During acute rhinitis, acute sinusitis, and the more active phases of allergic rhinitis, the pH of nasal secretion in situ is on the alkaline side, and then shifts back to the acid state when the stage of clinical resolution is reached. It is during the time of acute nasal embarrassment that the nasal mucous membranes are inflamed or congested, the secretions are increased, and nasal breathing itself becomes more labored. Nasal alkalosis takes place in response to the act of hyperventilation (blowing off of carbon dioxide), and this presumably can explain in part the reason for the

alkaline nasal state during acute rhinitis, acute sinusitis, and the more active stages of allergic rhinitis.

Intranasal treatment of the human nasal cavity by means of rational, physiological nasal medication requires not only treatment of mucous membrane surfaces (including ciliary action) but also treatment of nasal secretions (including the mucous blanket). Normal nasal secretion, including the mucous blanket, possesses a purposeful acid barrier against infection, for it has been observed that acidity as reflected in low pH values is unfavorable to the growth of pathogenic bacteria and that nasal secretion possesses an acid composition when receding after allergic attacks.

Nasal vasoconstrictors with an unusually high alkaline pH value disturb the normal nasal pH level present in clinically normal nasal passages and postpone the return of the nasal mucosa from a pathological alkaline status to a normal, slightly acid, status. During an attack of acute rhinitis, acute sinusitis, and the more active stages of allergic rhinitis, the employment of a nasal vasoconstrictor that lowers the abnormal alkaline pH in these conditions to a normal, slightly acid pH level between 5.5 and 6.5 in adults or 5.0 and 6.7 in infants and young children—in short, a physiological nasal pH—is most desirable in applied clinical practice.

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# DRUG SENSITIVITIES AND IRRITATIONS OF THE CONJUNCTIVA

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When the use of an eye medicament results in an untoward local reaction, the physician is apt to consider the reaction as allergic and alter treatment on this assumption. The fact that such drug intolerance might be due to direct irritation of the conjunctiva, rather than to a true sensitivity, may be overlooked. Actually, it may be postulated that irritative reactions to certain drugs are much commoner than allergies to these drugs. Such an assumption is especially true in regard to preparations of the alkaloids used in the treatment of glaucoma and uveitis. Drug irritations exhibit a clinical picture quite distinct from that of drug sensitivities and usually may be easily differentiated. The importance of this distinction lies in the fact that in drug irritations the use of the same drug may be continued if it is prepared in a manner that insures no more irritation, whereas in allergies an entirely different drug must be substituted. In certain conditions, such as glaucoma, where intolerance to miotics is not uncommon, it is sometimes not feasible to use another drug. On occasion, such a situation may result in a decision to resort to surgery. Investigation of the cause of this intolerance may permit control of the tension by the continued use of nonirritating preparations of the same miotic, if an allergy is not present. Before the concept of allergy was introduced, drug intolerance was generally ascribed to some form of irritation. Now that the vast scope and many manifestations of hypersensitivity are fully accepted, so many drug reactions are known to be due to contact allergy that not enough emphasis is being placed on the fact that drug irritations may occur. It is the purpose of this paper to consider the basic differences in these two types of drug reactions and attempt to delineate their clinical characteristics.

Reactive substances used as eye medicaments, like other drugs and chemicals,[1] may be divided into two classes: (1) primary irritants and (2) mucosal and cutaneous sensitizers. Some substances may act in both ways. Primary irritants cause an inflammatory reaction only by direct action and just at the site of contact. Inflammation occurs if the irritant is used in strong enough concentration, or in sufficient quantity, for a long enough period of time. Unlike an allergy, the irritation may develop the first time the substance is used. The conjunctiva and the very thin skin of the eyelids are both especially susceptible to the action of substances often not irritant elsewhere in the body. Persons with dry skins are especially prone to react to dehydrating chemicals. It is thought that the majority of occupational dermatoses are not allergic but occur in workers with anatomic or physiological skin defects or on excess contact in those who do not take proper precautions.[1] Primary irritants may, in addition, be sensitizers from the start or become sensitizers on intensive use. This fact explains some types of conjunctival drug reactions that occur where an allergy is superimposed on a drug irritation.

Mucosal or cutaneous drug sensitizers differ from irritants in that they act as true allergens. Thus, they do not generally cause reactions on first contact; instead, after approximately a week the entire skin, or all the mucous membrane, will react in a specific manner on further contact either at the original site or elsewhere. These are the sensitizing substances that cause contact (delayed) allergy, the type of ocular allergy best described as allergic dermatoconjunctivitis. While nonprotein substances are in themselves not primarily antigens, it is believed that they form true antigens in the body by union with the host tissues. These relatively simple chemicals, known as haptens, combine with body proteins, forming conjugates that act as antigens. The hapten confers specificity on the conjugate; hence, the allergy is directed against the hapten and not against the protein. This explains why the substitution of a drug that is chemically similar to one that previously caused sensitivity in a patient is dangerous. Thus, after allergy to one sulfonamide has developed, another sulfonamide is very likely to cause sensitivity.

Mr. Robert R. Feinstein aided in the preparation of this paper.

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1. Schwartz, L.: Allergy of the Skin, in Allergy in Theory and Practice, Cooke, R. A., editor, Philadelphia, W. B. Saunders Company, 1947, p. 263.

ALLERGIC CONJUNCTIVITIS

The following classification of allergic conjunctivitis is offered for purposes of reference:

1. Acute Allergic Conjunctivitis
   - Atopic (familial history of allergy)
   - Immediate allergic response (in a few minutes)
   - Positive intradermal test in 15 to 30 minutes
   - Due to inhalants, pollens, dusts, danders, feathers, or foods
   - Major characteristic: chemosis
2. Allergic Dermatoconjunctivitis
   - Delayed allergic response (24 to 48 hours)
   - Positive patch test in one to five days
   - Contact allergy due to drugs, cosmetics, chemicals, or apparel
   - Major characteristic: eczema
3. Chronic Allergic Conjunctivitis
   - A. Atopic Type
     - Immediate allergic response
     - Positive intradermal test in 15 to 30 minutes
     - Due to inhalants, pollens, danders, dusts, feathers, or foods
   - B. Bacterial Type
     - Delayed allergic response
     - Delayed positive intradermal test (24 to 48 hours)
     - Due to bacteria, fungi, and possibly viruses

*Allergic Dermatoconjunctivitis.*—Allergic dermatoconjunctivitis, the most frequently recognized type of conjunctival allergy, is basically a form of contact allergy, occurring 24 to 48 hours after exposure to an antigen. It is generally due to the local use of drugs, cosmetics, articles of clothing, jewelry, or chemicals used in industry. Itching is an important symptom as in all allergic conjunctivitis. The condition is characterized by: (1) eczema of the eyelids and the surrounding skin, (2) papillary conjunctivitis, and (3) conjunctival eosinophilia. Patch tests, using the responsible allergens, are often positive within 72 hours and are diagnostically valuable.

The eczematous reaction is, in almost all cases, the outstanding feature of the condition. Early mild cases may merely be characterized by slight dryness and thickening or abnormal wrinkling of the skin; usually, frank eczema occurs. It is not necessary for both eyelids to be involved simultaneously. Either the skin of the upper lid or that of the lower lid may be involved alone. This often provides a clue as to the etiology. When an allergic dermatoconjunctivitis is due to a drug, especially eye-drops instilled in the lower cul-de-sac, the earliest skin involvement may follow the usual paths of tear overflow, that is, the canthi and the adjacent lower lid skin. Allergy to ointments often first shows changes along the lid margins, which are swollen and inflamed but do not exhibit the scales and ulcers seen in typical blepharitis. Allergy due to cosmetics, especially nail polish and hair tonic or rinses, often first involves the skin of the upper lid. The conjunctival reaction may be severe. Generally a mucopurulent discharge occurs, resembling that noted in bacterial conjunctivitis. The conjunctivitis is characterized by papillary hyperplasia; isolated follicles occur rarely if ever and never dominate the picture the way they do in conjunctival irritation. Furthermore, the conjunctiva is diffusely and uniformly involved in the allergic inflammatory process. In conjunctival irritation, on the other hand, the major involvement is localized to the area of contact, usually the conjunctiva of the lower eyelid and the adjacent bulbar conjunctiva. The finding of eosinophils or basophils on epithelial scrapings is a very valuable diagnostic aid in the recognition of allergic dermatoconjunctivitis. They may not be present at the onset but usually appear if the reaction persists for several weeks.

Unlike the acute edematous type of allergic conjunctivitis, allergic dermatoconjunctivitis usually takes several hours to days to occur, even after sensitization has taken place, and disappears relatively slowly, in a matter of days or a week after the offending substance is eliminated. The diagnosis of allergic dermatoconjunctivitis when due to drugs is often easy. The clinical appearance, the history, and the finding of eosinophils in the secretion, followed by the beneficial effect of the elimination of the causal agent, makes a satisfying sequence of events. The recognition of other causes of this type of contact allergy is often more difficult.

It is important for the physician to differentiate allergic dermatoconjunctivitis from infectious eczematoid staphylococcic dermatitis. The latter condition may give a clinical picture resembling allergy very closely; in fact, the eczema that occurs, while presumably due to the dermonecrotizing toxin of the staphylococcus, may actually represent an allergic response to staphylococcus toxin. Many unrecognized cases of this type of staphylococcic infection are treated for long periods of time as cases of contact allergy. The intensive antistaphylococcic regimen, including the use of toxoids and vaccines, which often is required to cure the condition, is entirely different from that used in contact allergy. Infectious eczematoid staphylococcic dermatitis, as differentiated from allergic dermatoconjunctivitis, shows (1) blepharitis, often ulcerative, (2) a drier, more chronic type of papillary conjunctivitis with less discharge, (3) superficial epithelial keratitis involving the lower half of the cornea and seen best on slit lamp examination, (4) positive conjunctival and lid margin cultures showing numerous toxin-producing staphylococci, and (5) absence of eosinophils in epithelial scrapings.

Patch tests, where the suspected substance is applied to the skin and covered by an innocuous impermeable material kept in place by adhesive, are of value in contact allergy. When positive, a reaction generally appears after 24 hours; sometimes the patch must be left on longer. A negative patch test does not rule out the test substance as a causative agent because: (1) under the circumstances of the test the mechanism producing the reaction may be lacking, (2) the patient may no longer be sensitive, (3) the actual sensitizer is not applied, and (4) only a local sensitivity is present and the site of skin tested is not sensitive (a not infrequent occurrence). It is important that the test material not be too concentrated, as it then may act as a primary irritant, giving a false positive reaction. Thus in diagnostic testing for sensitivity to cosmetics it is better to apply the cosmetic daily in the way it is generally used, because in normal use the uncovered cosmetic loses much of its substance by evaporation. Patch tests do not permit this evaporation, so that cosmetics, harmless in actual use, may cause positive reactions.[1]

*Allergenic Drugs.*—Many ophthalmic drugs are true sensitizers. Contact allergy is most frequently encountered in the following groups:

Local Anesthetics: It appears that every local anesthetic used for instillation into the eyes is a potential sensitizer. Apparently every one in common use has been known to result in allergic dermatoconjunctivitis on occasion. Often, in the course of the treatment of external diseases of the eyes, it is customary to instill local anesthetics as a preliminary to other medication. It is surprising how frequently unsuspected allergy to these anesthetics is the reason for the inflammation becoming aggravated. Tetracaine (pontocaine®) hydrochloride, butacaine (butyn®) sulfate, dibucaine (nupercaine®) hydrochloride, and larocaine® (3-diethylamino-2,2-dimethylpropyl-*p*-aminobenzoate) hydrochloride are particularly prone to cause such allergies, which are often very severe. Cocaine hydrochloride, phenacaine ("holocaine") hydrochloride, and, possibly, piperocaine (metycaine®) hydrochloride are far less likely to, however, and should be used whenever an allergic factor is suspected.

Antibiotics: The tendency of penicillin to cause sensitivity is notorious. The high incidence of local reactions (up to 20%), especially when the drug is used in the form of an ointment, has tended to discourage its topical use. Furthermore, allergies due to the ocular use of penicillin are among the severest encountered with any medicaments. The high frequency of penicillin sensitivity may be related to previous sensitization of the skin by other fungus antigens, such as trichophytin, especially in adults. Ocular reactions have also followed the use of intramuscular penicillin, but they are generally not so severe. Urticaria due to penicillin may have a different mechanism, similar to that of serum sickness. Streptomycin is another frequent and potent sensitizer. Nurses get allergies after handling the drug, and their eyes are frequently affected. Dihydrostreptomycin, while not really less toxic, appears less often allergenic. Local streptomycin is often irritating to the eye. Of the other antibiotics, my personal experience would indicate that bacitracin is the least sensitizing; however, I have encountered some mild, and one moderately severe, instances of allergy following its use. It is possible that antibiotics derived from bacteria, such as bacitracin, are less allergenic than those derived from fungi. Thus sensitivities due to the local use of aureomycin, chloramphenicol (chloromycetin®), and oxytetracycline ("terramycin") occur more frequently. My experiences with the local use of neomycin and polymyxin have not been extensive enough, so far, to arrive at any conclusion concerning their sensitizing propensities.

Sulfonamides: All sulfonamide drugs are potent sensitizers when used locally, especially if this is prolonged. Although sometimes very severe, reactions are generally less serious than those encountered in allergies to the antibiotics and anesthetics. The newer sulfonamides, such as sodium sulfacetimide (sulamyd®) and sulfisoxazole (gantrisin®), cause fewer allergies than the original drugs in this group, such as sulfanilamide and sulfathiazole.

Ophthalmic Alkaloids: The mydriatic alkaloids often result in sensitization. Conjunctivitis due to atropine is usually a typical allergic dermatoconjunctivitis. Eczematous dermatitis, papillary hyperplasia, and a mucopurulent discharge, containing eosinophils and basophils, are all present. Under certain circumstances, however, atropine appears to act as an irritant and a follicular conjunctivitis develops, without dermatitis and eosinophilia. This manifestation will be discussed later. Both scopolamine hydrobromide and homatropine give rise to a similar allergic dermatoconjunctivitis. The miotic alkaloids, on the other hand, are rarely sensitizers. Prolonged use of pilocarpine or physostigmine ("eserine") salicylate generally produces a follicular conjunctivitis, with no dermatitis and eosinophilia, which is due to drug irritation, not drug allergy. A true allergic dermatoconjunctivitis does occur in rare instances; these cases, when associated with follicles, are explained by the fact that primary irritants may also be, or can become, sensitizers. Some instances, however, where follicles are absent, are due to a typical allergic reaction.

Other Commonly Used Ophthalmic Drugs: All mercurial antiseptic agents tend to cause allergic dermatoconjunctivitis, a limiting factor in their prolonged use. The fact that mercurials like sodium ethylmercurithiosalicylate (merthiolate®), nitromersol (metaphen®), mercuric oxycyanide, and phenylmercuric nitrate are frequently used as preservatives in ophthalmic solutions should also be remembered. Other preservatives like phenol derivatives, such as orthocresol, may likewise cause allergies. Ethylmorphine hydrochloride ("dionin"), argyrol® (mild silver protein), naphazoline (privine®) hydrochloride, zinc salts, boric acid, and even ophthalmic cortisone may cause ocular allergies. Ointment bases themselves may result in allergies, generally due to sensitivity to lanolin or petrolatum. In such cases the use of the active drug may be continued in another vehicle.

## IRRITATIVE CONJUNCTIVITIS

The immediate reaction of the conjunctiva to irritants may vary from hyperemia to necrosis depending on the strength of the irritant. Those irritants strong enough to cause severe, immediate reactions are not germane to this discussion. Conjunctival irritation due to ophthalmic medicaments first manifests itself by nonspecific chronic inflammation, with a watery discharge. Later, in some instances, proliferative changes and, particularly in the case of alkaloids and related drugs, the formation of follicles may then occur. The conjunctival involvement is less diffuse and less uniform than in allergy; often the area of most irritation, the lower lid and adjacent bulbar conjunctiva, bears the brunt of the involvement. There is no preauricular lymphadenopathy. Burning and irritation are major symptoms; there is little if any itching. The typical eczema of drug allergy does not occur. Skin patch tests are negative with these low grade conjunctival irritants; stronger irritants may give positive patch tests. Epithelial scrapings may reveal mononuclear cells but no eosinophils or basophils. This is different from the laboratory findings noted with severe chemical and vegetable irritants. Lime, ipecac, insect powders, indelible pencil, ricin, turpentine oil, and probably many

others result in an acute conjunctival reaction with massive eosinophilia, ranging up to 80% of all leukocytes.[2]

*Follicular Conjunctivitis Due to Ophthalmic Drugs.*—It has long been recognized that physostigmine salicylate, pilocarpine, and sometimes atropine may result in follicular conjunctivitis on prolonged use. Morax,[3] in his classical monograph on the subject of follicular conjunctivitis, classified this response under the heading of "toxic follicular conjunctivitis" but stated that a sensitivity (allergy) caused this reaction. He believed that the purity, concentration, acidity, and the sterility of the solutions played no role in the matter. Even at that time, however, there appeared to be a dissenting opinion; in 1925 Elschnig [4] had observed that the incidence of follicles due to these three drugs had lessened considerably ever since he had employed a preservative in their vehicles and thereby had checked bacterial contamination. The latter point of view coincides with my experience. It remained for Thygeson,[5] however, to point out the fundamentally different reactions that occur with pilocarpine and physostigmine salicylate, on the one hand, from that of typical allergic dermatoconjunctivitis. Thygeson felt that the follicular conjunctivitis due to these two drugs, unaccompanied by the itching, dermatitis, and conjunctival eosinophilia typical of allergic conjunctivitis, indicated a toxic follicular response and was not due to any allergy. My own investigations on this subject were stimulated by this excellent and sound differential of Thygeson but have led me to extend the hypothesis still further. It appears to me that the follicular responses observed with atropine, pilocarpine, physostigmine salicylate, diisopropylfluorophosphate (DFP), and neostigmine, as well as those that may occur with others of this group, are the reactions to the formation of irritating degradation products by a group of drugs that are particularly prone to deterioration unless prepared in solutions that will hinder or prevent such occurrences.

I prefer to consider this type of drug intolerance a form of irritative reaction, not a toxic one. In fact, it appears to me that follicular conjunctivitis of this type should be classified as irritative follicular conjunctivitis, along with similar instances of follicular conjunctivitis due to other recognized irritants. Repeated exposure to industrial irritants such as chemicals, dusts, and vapors results in irritative conjunctivitis, often complicated by the appearance of follicles. Moreover, while follicles could hardly be expected to occur in the more acute types of chemical irritation, they have nevertheless been seen in artificial or self-induced conjunctivitis. In fact, chronic irritative conjunctivitis due to repeated instillations of ipecac by malingerers has been at times confused with trachoma, owing to the numerous follicles that occur.[6] In mild cases the follicles only appear in the lower fornix; in severe cases the upper lid conjunctiva is also involved. The follicular responses to viral and bacterial toxins might even be considered as instances of toxic follicular conjunctivitis, as here biologically derived toxins are probably active. Perhaps the best example of this is molluscum contagiosum of the eyelids, where the virus is presumably not present in the conjunctiva but the toxin is.

Although both the terms toxic and irritative are only descriptive and do not indicate the ultimate mechanisms, which at the cell level may be similar, from a practical point of view the distinction is not an idle one. If the reaction is a toxic one, the drug must be discontinued, unless, in some way, its toxicity can be blocked; if a drug is only an irritant or cell stimulant due to deterioration, preventing such degradation will eliminate the drug intolerance and permit its continued use. I have observed clinically, as have others, that the use of such offending drugs may often be continued if these irritants are eliminated. Such observations would appear to offer strong evidence in favor of the above hypothesis. This does not mean that all cases of irritative conjunctivitis must exhibit follicles if the condition persists long enough. The occurrence of follicles as the result of any excitant depends in large measure on the susceptibility of the person with a lymphoid diathesis to react in such a manner. Thus, while certain viruses will result in follicles in almost everyone, other excitants such as bacteria and fungi as a rule do not do so but may do so in susceptible persons. Moreover, in folliculosis, despite the absence of any excitant, follicles may occur in the normal conjunctiva of children who show lymphoid hyperplasia elsewhere in the body. Allergic conjunctivitis rarely is characterized by follicles. I have encountered it in only two types of conjunctival allergy: (1) in allergic reactions to atropine and physostigmine salicylate, where an irritation preceded the allergy to both drugs, and (2) in long-standing chronic allergy, especially, the dry, irritative conjunctivitis due to hypersensitivity to staphylococcus toxin,[7] where other factors may operate in causing the folliculosis; however, follicles do not appear in significant numbers as compared to other forms of follicular conjunctivitis.

*Preparation of Nonirritating Ophthalmic Drugs.*—Drugs dispensed in ophthalmic solutions must be prepared in vehicles that will ensure their integrity over the period of use. Most important of all is the maintenance of the proper pH for that particular drug so that deterioration with formation of irritating degradation products will not occur. While extremes of the pH range in themselves are irritating, within reasonable limits of the normal pH of tears (7.0 to 7.4) the pH of a solution in itself is not a major consideration as far as the eye itself is concerned. Phosphate buffers should be avoided, as they may be both irritating and incompatible with certain alkaloidal salts. Boric acid–potassium chloride mixtures are advised. The importance of isotonicity is debatable. Since it is difficult to make a solution isotonic as well as buffered in all pH ranges, when employing active drugs the pH should be the prime consideration, since the buffer salts used automatically ensure an almost isotonic solution. Exceptions to this general rule include methyl cellulose and distilled water. Hypotonicity of a solution is more irritating than hypertonicity.

2. Theodore, F. H.: The Significance of Conjunctival Eosinophilia in the Diagnosis of Allergic Conjunctivitis, Eye, Ear, Nose & Throat Month. **30**: 653-656, 1951.

3. Morax, V.: Les conjonctivites folliculaires, Bull. et mém. Soc. franç. d'opht. **46**: 5-142, 1933.

4. Elschnig, A.: Conjunctivitis follicularis und Trachom, Klin. Monat. f. Augen. **74**: 9-18, 1925.

5. Thygeson, P.: Ocular Bacteriology, Boston, Ophthalmologic Study Council, 1947, p. 48.

6. Fromaget, C., and Harriet: Conjonctivites et pseudo-trachomes Provoqués par l'émétine, Ann. d'ocul. **153**: 388-395, 1916.

7. Woods, A. C.: The Diagnosis and Treatment of Ocular Allergy, Am. J. Ophth. **32**: 1457-1478, 1949.

Sterility of ophthalmic medicaments [8] is desirable because, in addition to the obvious danger of secondary ocular infection, contamination, even if nonpathogenic, may bring about alteration of the pH, deterioration of the drug, and the formation of bacterial end-products that, in themselves, may prove irritating. Preservatives used to maintain sterility must be also carefully chosen. *p*-Hydroxybenzoic acid esters, as well as benzalkonium chloride (cationic wetting agents), both frequently employed, may be irritating. Chlorobutanol is less likely to be an irritant. Ointment bases themselves may be irritants. Such irritations may be avoided if the pH is slightly alkaline.

*Irritation Due to Alkaloids and Related Drugs.*—Although the chemistry of the alkaloids is a very complex and not entirely understood subject, consideration of the degradation products of these relatively unstable drugs suggests a rational basis for the fact that they, as a group, have such a definite tendency toward a specialized reaction when irritation occurs. The most commonly used ophthalmic alkaloids and related synthetic drugs are considered from this point of view.

Generally, atropine reactions are typically allergic; however, cases of atropine irritation occur where a follicular conjunctivitis, without dermatitis and eosinophilia, is present. It is felt that the basis for irritation is the fact that atropine, itself a degradation product of hyoscyamine, unless properly prepared, will undergo further degradation to tropic acid and tropine,[9] which is a strong alkali. Final products are a group of esters known as tropeines. All these substances are irritants. Hyoscine (*l*-scopolamine) breaks down to atroscine, which further degrades like atropine. Homatropine breaks down to tropine and mandelic acid. Irritation is generally not encountered, because the drug is usually not prescribed for prolonged home use.

True allergy to pilocarpine is very rare. Pilocarpine intolerance is generally manifested by nonspecific irritative conjunctivitis, and less often by follicular conjunctivitis. Pilocarpine dissolved in distilled water has a pH of 4.9. Constant use over a long period of time of this acid solution may of itself prove somewhat irritating. Furthermore, degradation of pilocarpine results in the formation of irritating end-products such as acetic acid, propionic acid, ammonia, and methylamine,[10] which is a very strong base. The optimum pH for pilocarpine solutions is 6.9. The relief of irritations owing to pilocarpine hydrochloride by substitution of the nitrate salts may occasionally be successful, possibly because less degradation may occur. Sometimes the use of another, freshly or differently prepared, solution of the same salt may be beneficial. Generally, however, the best remedy for pilocarpine irritation is to use a properly prepared solution. The writer has noted personally on a number of occasions that such a solution will result in gradual disappearance of follicles and the relief of the irritative conjunctivitis. Others, to his knowledge, have had the same experience.

Physostigmine salicylate is much more prone to result in a follicular conjunctivitis than pilocarpine. Unless it is kept at an pH of 5.5 and an antioxidant such as sodium bisulfite is added, rapid deterioration occurs with change of color owing to the formation by oxidation of rubreserine and methylamine.[9] Because of its poor solubility, rubreserine crystallizes in needle-like crystals, which may also act as mechanical irritants. Further degradation, depending on the rate of oxidation,[11] results in either eserine brown or eserine blue (a strong base). All of these substances are chemical irritants. Physostigmine salicylate in oil is apparently less irritating than when prepared in distilled water, due to its increased stability, as may be physostigmine salicylate ointment. I have encountered several cases of physostigmine salicylate allergy with dermatitis and eosinophilia. In one, since follicles were also present, it was felt that, at first, a primary irritation occurred. Later, the irritant became a sensitizer, as mentioned early in the paper, and the allergy developed. In another case, no follicles were noted, indicating, perhaps, that irritation did not play a role.

Diisopropylfluorophosphate is a definite chemical irritant. In the presence of moisture, hydrofluoric acid and probably elemental fluorine are formed. Follicular conjunctivitis as a result of its use is not uncommon, occurring, like all the others in this group, with the absence of dermatitis and eosinophilia. The follicles, in one instance, disappeared after about one year, despite continued use of the same commercial product, although conjunctival injection and symptoms continued. Apparently tolerance developed, or else some lots are less apt to hydrolyze in the conjunctival sac. In another patient using the drug in peanut oil, a typical allergic dermatoconjunctivitis occurred with the absence of follicles. This was shown not to be due to diisopropylfluorophosphate itself but to a sensitivity to peanut oil.

I have encountered a follicular conjunctivitis of the irritative type, without dermatitis and conjunctival eosinophilia, due to the prolonged use of neostigmine in a patient with glaucoma, who previously had had a similar irritative follicular response to both pilocarpine and physostigmine salicylate. He was later able to tolerate other bottles of neostigmine for several years until irritation again developed, this time, however, without follicles. Since he had only one eye I did not wait till follicles developed but substituted buffered pilocarpine with good results. Compared to other miotics, neostigmine is quite stable in solution because hydrolysis is apparently minimal. On the basis of its chemical structure, when hydrolysis of neostigmine does take place it should result in the formation of dimethylamine, a very strong base, and 3-hydroxyphenyltrimethylammonium bromide. Perhaps in the case described, certain manufactured lots deteriorate more than others. Intolerance to furtrethonium iodide has been noted to cause thickening of the conjunctiva, especially of the lower fornix [12]

8. Theodore, F. H., and Feinstein, R. R.: Practical Suggestions for the Preparation and Maintenance of Sterile Ophthalmic Solutions, Am. J. Ophth. **35**: 656-659, 1952.

9. Henry, T. A.: The Plant Alkaloids, ed. 4, Philadelphia, Blakiston Company, 1949, pp. 72, 540.

10. Jowett, H. A. D.: The Constitution of Pilocarpine, J. Chem. Soc. London **79**: 1331-1346, 1901; **83**: 438-464, 1903.

11. Salway, A. H.: Researches on the Constitution of Physostogmine, J. Chem. Soc. London **101**: 978-989, 1912.

12. Scheie, H. G.: The Treatment of Primary Glaucoma by Medical Means, Tr. Am. Acad. Ophth. **53**: 186-212, 1949.

and dacryostenosis owing to proliferative changes. There is little itching. This would indicate an irritative process. On the basis of its chemical composition, which is similar in some ways to physostigmine salicylate and neostigmine, it appears that methylamine would be one of the degradation products.

In summary, it appears likely that the basis for the irritative follicular conjunctivitis that is characteristic of the ophthalmic alkaloids is the formation of irritant degradation products. These may largely be prevented by employing suitable means of preparation. It is interesting to observe that all the miotic alkaloids and the synthetic miotics discussed above, as well as methacholine (mecholyl®) and carbachol (choline chloride carbamate), contain methylammonium radicals that apparently break down to methylamine or dimethylamine. Whether this is of any special significance cannot be stated at the present time.

## TREATMENT

The best treatment of drug allergy is to eliminate the offending medicament and use, if necessary, another drug having a similar pharmacological action. The drug substituted should differ as much as possible chemically from the original excitant, because once sensitization to a drug is evoked allergies to related drugs are more prone to occur. The drug chosen should also be the least likely to sensitize of all the medicaments available for the purpose, because when an allergy occurs many drugs ordinarily harmless to the patient may act as allergens. Furthermore, even in the absence of an allergy, if an allergic background or history exists, the choice of the drug initially used should be based on these criteria. Serious and permanent sequellae have occurred following the indiscriminate use of highly allergenic antibacterial agents. These could have been avoided by the use of other equally useful, but safer, medicaments. If it is necessary to continue the use of a drug, such as atropine in uveitis, the concomitant administration of sufficiently large amounts of cortisone or corticotropin (ACTH) systemically is advised. Often, but not always, the local use of ophthalmic cortisone will suffice, permitting the continuance of the allergenic medicament; however, a definite quantitative dosage factor exists in regard to these hormones and must be kept in mind. Antihistamines, both systemically and locally, have not proved valuable, in my experience, in allergic dermatoconjunctivitis.

The treatment of irritative conjunctivitis due to drugs is the use, if possible, of properly prepared solutions that will not result in degradation of the active drug into irritating end-products. Such solutions are commercially available or else may be made up by pharmacists. Adjuvant use of cortisone or corticotropin may sometimes be necessary but is less valuable than in allergies. Where a drug, such as diisopropylfluorophosphate is the only one effective and must be used as supplied by the manufacturer, it has been found by me that the patient may continue to use the drug for long periods of time without deleterious effects other than the persistence and the increase of the follicles. As noted above, sometimes the patient apparently becomes more tolerant to the drug irritants upon prolonged use, so that the symptoms are less intense and the follicles may even disappear.

## SUMMARY

Although most instances of ocular drug intolerance are due to drug allergy, enough cases of drug irritation occur to make it an important consideration. Drug sensitivity is a form of contact allergy and is characterized by itching, dermatitis, catarrhal conjunctivitis, and conjunctival eosinophilia or basophilia. Certain groups of drugs are especially prone to become sensitizers. These include local anesthetics, antibiotics, sulfonamides, mydriatic alkaloids, and mercurials. When allergic dermatoconjunctivitis develops it generally requires elimination of the responsible drug.

Drug irritants cause reactions by direct conjunctival irritation. While some drugs are themselves primary irritants, and almost every drug may at times be irritating, those clinically important are the ones that are used regularly over long periods of time and whose preparations are prone to deteriorate into irritating degradation products if not prepared in a manner that will hinder or prevent this breakdown. The alkaloids, especially the miotics, as well as other chemically related medicaments are particularly apt to do this. The clinical picture of irritative conjunctivitis due to drugs is generally a nonspecific watery conjunctivitis, without dermatitis or eosinophilia. In chronic cases, especially with use of the alkaloids, follicular conjunctivitis is the outstanding occurrence. There are a number of general factors such as the hydrogen-ion concentration that should be considered in the compounding of nonirritating preparations of any ophthalmic drug. These are especially important in regard to the ophthalmic alkaloids and related synthetic miotics. Consideration of the degradation products of this entire group of drugs reveals not only that they more readily tend to form irritative end-products, but that, in many instances, these irritating end-products are similar.

Since drug irritation can be avoided by using properly prepared solutions of the same drug, while drug allergy requires substitution of a different drug, it is of great importance at times to make the distinction between these two types of drug intolerance.

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**Immunization in Infancy.**—When immunization is planned for a child who has a history of previous febrile convulsions, it is perhaps best to give fractional doses of antigen, beginning with 0.1 cc. Some physicians routinely administer acetylsalicylic acid in a dose of 1 grain (65 mg.) per year of age every four hours for a day or two after immunizing injections.

It is always wise to question the mother in regard to the occurrence of any febrile, convulsive, local or other reaction to the previous injection when the child is brought in for the second and subsequent injections. If a convulsion or severe reaction has occurred, subsequent injections should be postponed for at least a year. Then I would favor omission of the pertussis antigen. A number of cases have been reported in which an encephalitic type of reaction followed an injection of pertussis antigen in twenty minutes to seventy-two hours. In some of these infants the reaction, manifested by fever, drowsiness and convulsions, was observed after the first injection. Only six of the fifteen infants observed by Byers and Moll made a satisfactory recovery after such reactions.—George B. Logan, M.D., Immunization During the First Year, *Minnesota Medicine*, September, 1952.

# TUBERCULOUS TENOSYNOVITIS

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The sheaths of tendons are an uncommon site of tuberculous involvement as compared to other parts of the body, but tuberculous synovitis occurs often enough to warrant particular attention and study. The condition, in addition, is quite disabling to the patient, and, like tuberculosis elsewhere, is likely to be a slow and progressively destructive process in spite of the usual conservative management. In regard to surgical treatment, it has been pointed out by Adams and co-workers [1] that it is unusual that tuberculosis, a recognized nonsurgical disease, should be attacked so avidly by operations on the tendon sheaths. Nevertheless, reports in the literature bear out the frequency of the surgical approach, and it was with this in mind that a study of this disease process, especially in reference to the results from surgical excision, was attempted.

## MATERIAL AND METHOD

The basis for this study was a group of patients with a diagnosis of tuberculous tenosynovitis who were treated at the Mayo Clinic. The microscopic features were reviewed, and all cases in which there was no evidence of tuberculosis were omitted. A few cases, in which the diagnosis was made clinically, treatment was conservative, and pathological material was not available, were studied but placed in a separate group. The clinical features of this disease were tabulated in an attempt to correlate the physical findings and history with the gross findings at operation and with the clinical results. The main emphasis was placed on the surgical approach to the problem and an evaluation of the results obtained with this method as compared to conservative or nonoperative treatment.

The entire group of cases was classified according to the various criteria used to establish the diagnosis. In the cases in which pathological material was available, previously made slides were recalled and studied and new sections were made when indicated. The cases were classified according to the basis used for diagnosis as indicated in table 1.

Following the classification according to the basis used for diagnosis, the entire group was broken down into two series. Series 1 consisted of subgroups, C, D, and E (table 1), representing patients with proved tuberculosis. There were 37 patients in this series, of whom 35 were treated surgically and 2 conservatively. Series 2, consisting of subgroups, A, B, C, D, and E (table 1) was also studied to a less extent. There were 52 patients in this series, of whom 37 were treated surgically and 15 were treated conservatively.

## CLINICAL OBSERVATIONS

The exact incidence of tuberculous tenosynovitis is not known, but that it is uncommon is evidenced by a survey of the literature. In 1940, Adams and co-workers [1] reported 36 cases from the Massachusetts General Hospital covering a period of 45 years, and stated that the incidence was 1 per 7,891 admissions. Steindler,[2] in 1936, reported 24 cases in which the tendons of the wrist were affected, and Bunnell [3] reported a personal series of 21 cases in which the condition was treated surgically. Our series covers the period 1915 to 1949 inclusive, the great majority of the cases occurring since 1930.

The sex distribution is generally reported to be in the ratio of approximately three males to two females. In our series 1 (proved tuberculosis) there were 19 males to 18 females, and in series 2 (all cases including those in which a clinical diagnosis only was made) there were 28 males to 24 females (table 2). According to the literature, the average age of the patients is 35 to 40 years. In our group the youngest patient was 19 years of age and the oldest was 73; the average age in series 1 was 44.1 years and in series 2 it was 41.7 years.

TABLE 1.—*Basis for Diagnosis and Type of Treatment*

| Subgroup | Basis for Diagnosis | No. of Cases | Type of Treatment: Conservative | Type of Treatment: Surgical |
|---|---|---|---|---|
| A | Clinical impression only | 6 | 4 | 2 |
| B | Clinical impression supported by presence of tuberculosis elsewhere in the body | 9 | 9 | 0 |
| C | Positive histological evidence | 28 | 1 | 27 |
| D | Positive bacteriological evidence only | 0 | 0 | 0 |
| E | Positive histological and bacteriological evidence | 9 | 1 | 8 |
| F | Proved not to be tuberculosis | 11 | 2 | 9 |
| | Total ..... | 63 | 17 | 46 |

The onset of this condition is characteristically gradual and insidious, with a slowly progressive swelling in the involved part followed by pain and limitation of motion. Bunnell [3] states that the symptoms at first are so mild that the disease is often well advanced, even of several years' duration, before the patient comes for treatment. In our group, the duration of symptoms before the patient was first seen varied from 11 days to 20 years; the average duration in series 1 was 45.2 months and in series 2 it was 38.7 months. In the cases in which there was a long period before treatment, the symptoms were mild and only slightly disabling, and the patient did not seek relief until the symptoms had become rapidly progressive.

Bunnell [3] stresses the frequent incidence of this condition in persons who work with cattle, such as milkers,

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1. Adams, R.; Jones, G., and Marble, H. C.: Tuberculosis Tenosynovitis, New England J. Med. **223**: 706-708 (Oct. 31) 1940.
2. Steindler, A.: Tuberculous Tenosynovitis of the Wrist, J. Iowa M. Soc. **26**: 142-144 (March) 1936.
3. Bunnell, S.: Surgery of the Hand, ed. 2, Philadelphia, J. B. Lippincott Company, 1948, pp. 754-761.

skinners and butchers, and particularly in those who work with diseased cattle. He suggests that the disease is probably most commonly of the bovine type. Adams and co-workers [1] mention the occupations of their patients, and indicate that the large number of laboring persons in the series likely means that hard use of the hands is probably a predisposing factor. In our group of cases the occupations of the patients were not tabulated, but a history of exposure to tuberculosis was elicited in 16 of the 37 cases in series 1 and in 26 of the 52 cases in series 2. Trauma is also mentioned quite frequently as a predisposing factor in the onset of this condition, but its exact relationship has never been accurately determined. In series 1, 14 of the 37 patients gave a history of trauma, and in series 2, 17 of 52 patients gave such a history.

TABLE 2.—*Summary of Clinical Data*

| | Series 1 * | Series 2 † |
|---|---|---|
| **Sex** | | |
| Males | 19 | 28 |
| Females | 18 | 24 |
| **Age, yr.** | | |
| Youngest | 22 | 19 |
| Oldest | 73 | 73 |
| Average | 44.1 | 41.7 |
| **Duration of symptoms before first seen** | | |
| Shortest, days | 11 | 11 |
| Longest, yr. | 20 | 20 |
| Average, mo. | 45.2 | 38.7 |
| **History of trauma** | 14 | 17 |
| **History of exposure to tuberculosis** | 16 | 26 |
| **Tuberculosis elsewhere in body** | 14 | 23 |
| Lungs | 10 | 16 |
| Kidneys | 2 | 3 |
| Skeleton | 5 | 6 |
| Cervical lymph nodes | 0 | 2 |
| Skin | 0 | 1 |
| Epididymis | 0 | 1 |

* Proved tuberculosis.
† Both proved and clinically diagnosed tuberculosis.

TABLE 3.—*Sites of Involvement in Tuberculous Tenosynovitis*

| Tendons Affected | Series 1 | Series 2 |
|---|---|---|
| **Wrist** | | |
| Total cases | 26 | 37 |
| Right | 18 | 25 |
| Left | 8 | 12 |
| Flexors | 21 | 27 |
| Extensors | 2 | 6 |
| Both | 3 | 4 |
| **Hands** | | |
| Total cases | 12 | 15 |
| Right | 8 | 10 |
| Left | 4 | 5 |
| Flexors | 9 | 10 |
| Extensors | 2 | 4 |
| Both | 1 | 1 |
| **Foot and ankle** | | |
| Total cases | 9 | 13 |
| Right | 6 | 7 |
| Left | 3 | 6 |
| Extensors | 5 | 8 |
| Peroneals | 5 | 7 |
| Posterior tibial | 1 | 1 |
| Achilles | 1 | 1 |
| **Long head of biceps tendon** | 1 | 1 |

The tendons of the wrist are by far the most commonly involved structures, and further extension along the synovial sheaths to the hand is a common sequela. Bunnell [3] states that the "right hand is affected about twice as often as is the left, and the volar tendons about twice as frequently as the dorsal ones." Our group of cases is similar in this regard, inasmuch as the right wrist was involved 18 times and the left 8 times in series 1. The sites of involvement in both series are shown in table 3.

The symptoms are rather characteristic in that they are insidious in onset and are first manifested by a slowly progressive swelling. The swelling may start in the tendon of a finger and progress up through the palm into the tendon sheaths of the wrist, but is most commonly seen first in the wrist. In the early stages the mass can be more readily localized to the course of the tendon sheath involved and is of a firm, doughy character. Later the mass becomes more generalized as more tendons are affected, and it may have a semifluctuant feeling. In the stage of extreme chronicity and in the presence of rice bodies, the semifluctuant mass may be pressed back and forth beneath the annular ligament, and rice bodies, if present, may give a crepitant feeling.

Pain and tenderness are not usually severe but are second in frequency of symptoms. A visible inflammatory condition of the skin and overlying structures is unusual, and tenderness is not marked, as it may be in pyogenic infections. A feeling of stiffness of the affected part is next in frequency, and, although commonly complained of, is not usually of an incapacitating nature. Paresthesias and numbness, especially due to pressure on the median nerve, which are manifested in the index, ring and middle fingers, are not uncommon, and weakness of grip is a frequent complaint.

TABLE 4.—*Prominent Symptoms of Tuberculous Tenosynovitis*

| Symptom | Series 1 | Series 2 |
|---|---|---|
| Swelling | 37 | 52 |
| Pain | 22 | 28 |
| Stiffness | 13 | 18 |
| Crepitation | 5 | 5 |
| Paresthesias or numbness | 6 | 6 |
| Weakness | 5 | 6 |

The constitutional symptoms usually present in tuberculosis involving other parts of the body are notoriously lacking except in cases in which there is generalized tuberculosis. Table 4 shows the incidence of the prominent symptoms in our group of cases; in the 37 cases of proved tuberculosis (series 1) swelling was universally present. The distribution of symptoms was similar in series 1 and in series 2, which included the cases in which the disease was diagnosed by clinical methods only. In 13 of the 37 cases of series 1, rice bodies were found at operation.

Laboratory studies are not of great importance, because the diagnosis is usually made both pathologically and bacteriologically from material obtained at operation. Nevertheless, the results of some of the more pertinent procedures are of interest in this series of cases. In series 1, roentgenograms of the thorax of 35 patients were made; 12 of these gave positive evidence and 23 gave negative evidence of tuberculous involvement of any degree (table 5). Tuberculin skin testing was done in 9 of the 37 cases of series 1, and in 6 of these the results were positive and in 3 they were negative. Sedimentation

rates, according to the Westergren method, were determined in 30 cases of series 1; in 19 cases the rate was more than 20 and the average reading for the series was 32.1 mm. in one hour. It is interesting to note that in series 1 (proved tuberculosis) agglutinations for Brucella organisms were performed in two cases, and in both the results were negative. In two of the cases of series 2 (both proved and clinically diagnosed tuberculosis), the agglutinations for Brucella were positive. Unfortunately, operations were not performed in these cases, and pathological material therefore was not available. The inference, however, is that infection of the tendon sheath by Brucella organisms may manifest itself clinically in a way similar to that of tuberculous tenosynovitis. Guinea pig inoculations were performed in 11 cases, in 7 of which the results were positive. In four the results were negative, but the disease proved to be tuberculous on pathological examination. Cultures for tubercle bacilli were made in nine cases, the results of which were positive in five and negative in four. Smears from surgical specimens were examined for tubercle bacilli in 10 cases; the results were positive in 4 and negative in 6 cases.

Although an unequivocal diagnosis of tuberculosis cannot be made histologically, our experience indicates that typical caseous granulomatous lesions in tendon sheaths are almost always tuberculous. This series demonstrated also that a culture or guinea pig inoculation for tuberculosis may give falsely negative results if the sample examined is inadequate.

In the series of 37 cases of proved tuberculosis, roentgenograms of the involved part were made in all cases, and four of these showed definite involvement of bone. In 21 cases there was roentgenographic evidence of soft-tissue swelling, and in 14 cases the results of roentgenologic studies were negative. The microscopic appearance was studied in all cases in which material was available, and, as indicated previously, new sections were made when indicated. The pathologist had no clinical history or findings available prior to his diagnosis, and, in all cases in which the bacteriological findings were positive, the histological examination was made concurrently. In 11 of the 63 cases studied, the disease was proved not to be tuberculosis; in 4 of the 11 cases the disease proved to be nonspecific synovitis and in 3 it was classified as rheumatic tenosynovitis. In one case in which a diagnosis of caseous tuberculosis had been made previously, examination of recut sections from the same material proved the disease to be of a rheumatoid nature.

## RESULTS OF TREATMENT

The great majority of the patients in our group of cases were treated surgically by extensive and tedious complete synovectomy and excision of surrounding tuberculous tissue. No cases in which simple drainage was performed were included in the surgical evaluation.

An attempt was made to contact all the patients and to obtain follow-up data. Of the surgically treated patients in series 1 (proved tuberculous tenosynovitis), follow-up data were available on 30. The average follow-up period was 6.5 years, the longest being 18 years and the shortest 1 year. The patients were questioned concerning the condition of their general health, the amount of pain and swelling in the involved part, the presence or absence of drainage, and the status of motion in the affected part. In addition, they were questioned as to the amount of restriction of activities of the part and the recurrence of the process, either in the same or a different part of the body.

The results of the follow-up study were classified as excellent, good, fair, or failure. The results were considered excellent if the patient's general condition was good, there was no recurrence of the process, there was no pain or swelling or drainage, there was unrestricted or markedly improved motion and no restriction of activities, and no further treatment was necessary; there were eight cases in this category. The results were classified as good if the patient's general condition was good with no recurrence of the process, the pain and swelling was improved or absent, there was no drainage, there was improved motion since operation, and there was no restriction or only slight restriction of activities; there were 11 cases in this category. In four cases the results were classified as fair; in these cases the status of the swelling, motion, and pain was only slightly improved, there was no drainage, there was some restriction of activities of the part, but there was no definite recurrence of the process. There were seven failures, in which there was reported definite recurrence of the process with further surgical procedures being necessary; in these cases either osseous involvement or drainage developed, or the condition became worse after operation. The seven failures represented definite recurrence, and, among these, there were four cases in which destructive arthritis developed and necessitated arthrodesis of the involved joint. Further excision of tissue at the site of the tuberculous tenosynovitis was carried out in four of the cases, which were classified as failures.

TABLE 5.—*Laboratory Data in Two Series of Cases of Tuberculous Tenosynovitis*

| | Series 1 | Series 2 |
|---|---|---|
| Roentgenogram of thorax | | |
| Positive | 12 | 18 |
| Negative | 23 | 30 |
| Tuberculin skin test | | |
| Positive | 6 | 11 |
| Negative | 3 | 3 |
| Sedimentation rate | | |
| Total cases | 30 | 37 |
| Average reading, mm./hr. | 32.1 | 34.1 |
| Cases in which reading was more than 20 mm./hr. | 19 | 23 |
| Roentgenogram of involved part | | |
| Total cases | 37 | 48 |
| Bone involved | 4 | 7 |
| Soft-tissue swelling | 21 | 25 |
| Normal findings | 14 | 21 |
| Agglutination for Brucella | | |
| Positive | 0 | 2 |
| Negative | 2 | 2 |
| Guinea pig inoculation | | |
| Positive | 7 | 7 |
| Negative | 4 | 7 |
| Cultures for tubercle bacilli | | |
| Positive | 5 | 5 |
| Negative | 4 | 7 |
| Smears for tubercle bacilli | | |
| Positive | 4 | 4 |
| Negative | 6 | 8 |

It is interesting to note that four of the eight patients who obtained excellent results received a course of streptomycin therapy following operation. Streptomycin therapy was received also by 3 of the 11 patients who obtained good results, 1 of the 4 who obtained fair results, and 2 of the 7 who represented failures. All patients receiving streptomycin reported improvement, even

though the process may have recurred at a later date. The majority of the patients who did not receive streptomycin were treated before this drug was available.

The presence of active tuberculosis elsewhere in the body reflected somewhat the ability of the patient to control the disease after surgical treatment. This is indicated by the fact that five of the seven patients who represented failures and only three of the eight who obtained excellent results had involvement elsewhere. Of the last-mentioned three patients, one had old fibrous tuberculosis of the lung classified as inactive and one had had a previous arthrodesis of a tuberculous knee and a roentgenogram of the thorax that did not disclose any abnormality. Only 4 of the 11 patients with good results and 1 of the 4 with fair results had tuberculosis elsewhere.

The evaluation of conservative treatment of tuberculous tenosynovitis was difficult in our group of cases, mainly because the diagnosis depended primarily on the study of material obtained at operation. Material obtained from aspiration and surgical procedures elsewhere was the basis for diagnosis in two of the cases included in series 1 (proved tuberculous tenosynovitis). In both of these cases the patients were treated conservatively with casts and supportive measures, but, unfortunately, follow-up information was not obtained in either case.

Three patients with proved tuberculous tenosynovitis were treated conservatively when first seen. In one of these cases the disease process involved the flexor tendons of the right wrist, with pressure on the median nerve. This was treated primarily with roentgen rays and immobilization, but the condition became worse and an operation was performed later. In this case the result was classified as a failure of primary surgical treatment because reoperation was necessary two years later; however, a query five years after the second operation revealed that the patient's general health was good and the condition of the wrist was much better, with no drainage, less pain and swelling, and considerably more motion. There were no restriction of activities and no similar condition elsewhere in the body.

The second patient who had proved tuberculous tenosynovitis and who was treated conservatively when first seen, underwent diagnostic aspiration, along with immobilization. The condition became worse, however, and surgical excision was necessary one year later. The results of both pathological and bacteriological studies were positive for tuberculosis. This patient received both penicillin and streptomycin postoperatively, and a follow-up study three years later disclosed that the patient's general health was good. The swelling and pain in the wrist had completely disappeared, the motion was better, there was no drainage, and the patient reported that there was not too much restriction of activities. It is interesting that this patient gave a history of symptoms for approximately 25 years, during which time simple surgical drainage procedures had been of no avail. The condition had become suddenly much worse a few months before the patient was seen at the Mayo Clinic.

The third patient who had proved tuberculous tenosynovitis and who was treated conservatively when first seen had involvement of the long head of the biceps tendon. Aspiration and roentgen therapy produced no improvement, and surgical excision was necessary. At the time of operation many rice bodies were found extending 5 in. (13 cm.) along the course of the tendon, and both pathological and bacteriological studies gave positive results. Unfortunately, the patient could not be traced, and no follow-up data for comparison of the two types of treatment were available.

Follow-up data were available in only five of the cases in which treatment was conservative and in which the diagnosis of tuberculous tenosynovitis was based on clinical impression supported by the presence of active tuberculosis elsewhere in the body. In one of these cases, in which flexor tendons of the left wrist were affected, a six-year follow-up revealed the condition to be still present, but no drainage was reported. In another case in which the extensor tendons of both wrists were affected, the condition spread to the volar aspects of the right wrist and the tendons on the dorsum of the left foot became involved six years later. Ten years later the condition was reported as still present but, in general, better. The pain and motion of the involved parts were reported as the same. No drainage was present. In another case in which the flexor tendons of the left wrist were the site of the disease, a follow-up investigation five years after the patient was first seen revealed that the condition had progressed for three years and that complete synovectomy had been necessary elsewhere; the result was excellent. In another case, in which the peroneal tendons of the right ankle were affected, there was improvement after four years of conservative treatment. In the final case, in which treatment was conservative and in which the right wrist and left ankle were affected, follow-up studies about 15 years later disclosed that the patient had no complaints referable to the disease; this must be considered a good result. In general, conservative treatment was not successful in relieving the conditions, and later surgical treatment was usually necessary.

It has been thought that the best surgical results are obtained in those cases in which the disease process is less active. In view of this, an attempt was made to correlate the pathological findings with the end results of surgical treatment. The presence of rice bodies has been felt to indicate a stage of chronicity. In our group rice bodies were found in 11 cases in which follow-up data were available. Three of the 11 patients had excellent results from treatment, 2 had good results, 3 had fair results, and 3 had failures. Thus, no correlation was evident. Also, there was no indication that the amount of caseation necrosis as observed by the pathologist had any correlation with the end results of excision.

## SUMMARY AND CONCLUSIONS

A study was made of 52 cases of tuberculous tenosynovitis. In 37 of these cases the diagnosis was proved correct by the results of histological and bacteriological examination; in the other 15 cases the diagnosis was based on clinical impression only. On the basis of this study the following points are made:

1. Tuberculous tenosynovitis is a chronic, slowly destructive disease, which, oddly enough, responds much better to open operative excision of the affected tissue than it does to the conventional treatment of tuberculosis, namely, rest of the part by immobilization and sup-

portive care. 2. Almost any long tendon or group of tendons may be involved but the wrist is by far the commonest site. 3. The tendons on the right side of the body are affected about twice as often as are those on the left, probably because of increased trauma and use. 4. Our cases were about equally distributed as to sex, in contradistinction to the approximate ratio of 3 males to 2 females reported in the literature. 5. No correlation between the pathological process and the surgical end results could be obtained. 6. Complete excision of the tuberculous mass while it is still limited to the tendon sheaths and before the disease process has spread to the surrounding structures, especially bones and joints, is the treatment of choice.

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# STATE HEALTH ORGANIZATION TODAY AND A DECADE AGO

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*and*
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Some 10 years ago a paper was read before the Section on Preventive and Industrial Medicine by one of us (J. W. M.). It was entitled "A Plea for Unity in Health Administration at the State Level," and was based on conclusions derived from the 1940 decennial survey of state health organization made by the United States Public Health Service. The findings reported here are derived from the 1950 survey. The first such comprehensive survey of state health departments was made under the auspices of the American Medical Association by Dr. Charles V. Chapin in 1915.

Unlike Chapin's survey, which focused on the health department only, those of the U. S. Public Health Service in 1940 [1] and in 1950 [2] included the entire spectrum of health services, environmental, personal, preventive, remedial, and custodial, administered by any and all official state agencies. Our current data provide clear evidence that the plea for unity following the 1940 survey was in vain. In the past decade, further dispersion of health functions throughout the structure of state government has gone on apace.

The current study reveals first, a maze of official agencies in each state, with wide scattering of responsibilities for health programs throughout the maze; second, a state-to-state difference in the configuration of agencies responsible for specific functions; and third, state-to-state variation as to degree of responsibility for those functions. For the nation as a whole, exclusive of organizations differing in name only, there are 60 distinct types of state agencies carrying on health functions. In 1940, there were 48 such types of agencies. The maximum number of agencies participating in health services in any one state in 1940 was 18; today it is 32.

This increased interest in health activities is most accentuated in the newer health fields. Accident prevention, for instance, claims the interest of 13 official agencies in one state. To name just a few typical agencies in this field, we might mention the departments of education, welfare, industrial relations, agriculture, public safety, and mental hygiene, and the public utilities commissions. All have their special and obvious interests—sometimes intertwined, sometimes overlapping, sometimes completely separated from the health department's own program for accident prevention.

We might also review briefly the scattered responsibilities for the recently organized heart disease control programs. The state health department most frequently provides preventive and educational services, and subsidizes local health activities. In about half of the states and territories providing hospitalization, the health department is the agency that administers the hospitalization and usually clinic services as well, chiefly for eligible rheumatic fever patients. However, in the other half, the state university oftenest is the chief agency providing one or both of these functions, with responsibility for rehabilitation services usually centered in the state's department of education.

Other programs concerned with personal health follow similar patterns, especially those providing medical care to indigent and categorical groups, or offering crippled children's and cancer control services. Here, again, agencies other than the health department participate. Some typical ones are the university hospital, the departments of welfare, education, and labor, workmen's compensation boards, and industrial and insurance commissions. Although agencies involved in medical care functions have made some effort to cooperate, no consistent system of official coordination has been instigated. Recent federal legislation affording more liberal provisions for medical care of public assistance clients points up the need here for closer integration.

Another factor accenting health program differences is the degree to which the states delegate responsibility to local areas. In some states, practically all responsibility for specific phases of activities is delegated to local units, with state agencies retaining only regulatory or consultative functions. Other states retain supervisory control, provide local grants, or operate direct service units. States often employ varying combinations of these methods.

Some attempts at integration have been made. For instance, a number of states are drawing together the var-

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† Dr. Mountin died April 26, 1952.

Read before the Section on Preventive and Industrial Medicine and Public Health at the 101st Annual Session of the American Medical Association, June 12, 1952.

From the United States Public Health Service. Assistant Surgeon General and Chief, Bureau of State Services (Dr. Mountin); Medical Director and Chief, Division of State Grants, Bureau of State Services (Dr. Haldeman).

1. Mountin, J. W., and Flook, E.: Distribution of Health Services in the Structure of State Government, Bulletin 184, ed. 3, Federal Security Agency, United States Public Health Service, 1943.

2. Mountin, J. W.; Flook, E., and Minty, E. E.: Distribution of Health Services in the Structure of State Government, 1950: Administrative Provisions for State Health Services, Bulletin 184, ed. 4, Federal Security Agency, United States Public Health Service, 1952.

ious state agencies performing water pollution control functions by forming "water boards" or "stream pollution commissions" for joint policy making, planning, and coordination of activities. In states where the health department is the designated water pollution administrator, the chief engineer frequently acts as agent.

In more than one-half of the states joint committees have been formed between representatives of the state boards of health and education to plan, administer, and coordinate school health services. In others, the governor has organized interagency committees to coordinate official activities and to study problems that cut across the functions of several state agencies. Moreover, in a few of the better established health programs, efforts have been made to transfer specific functions from other departments to the state health agency. For example, in eight states tuberculosis sanatoriums controlled by the department of welfare or by tuberculosis boards or commissions in 1940 are now operated directly by the state health department.

The steady extension of interest in health matters reflects not only general public enlightenment but also the advances made in this decade in scientific knowledge and resources. Moreover, medical advances have simplified or eliminated many of the earlier public health problems, leaving opportunity for state health and other agencies to branch out into new fields and ideas. From this standpoint, state health activity is progressive. More than half of the programs in the current survey are carried on in all the states and territories by at least one official state agency. This degree of responsibility among the states did not exist in 1940, when less than one-third of the programs were carried out in each of the states. Today, the only activities in which fewer than three-fourths of the states participate are some of the newly established chronic disease programs, hygiene of housing, human blood and blood derivative programs, and health services for migratory labor.

Some progress has been made in concentrating the older and better established programs within health departments. Nevertheless, our findings indicate that too many areas have failed to utilize, especially for the more recent programs, the extensive authority, the technical skills, and the basic interest in total health available in the health department. Organizationally speaking, the new functions appear to have been fitted into or tacked onto the administrative framework of state government without system or design. Is it necessary for new programs to go through this chaotic stage? Can we examine these programs and capitalize on the administration experience gained from older services?

Now for the time being, let us drop integration and its opposite, dispersion. Perhaps more revealing criteria of change are expenditures, functions, and personnel. The changes in scope and distribution of state health services are reflected in the differences in expenditures in the two most recent survey years. Estimated total health expenditures for the preventive services, hospitalization, and medical care provided by the 48 states in 1950 were approximately one billion dollars, or about $6.30 per capita. These amounts are more than three times larger than corresponding figures reported for 1940. Of the current total, 74% was state appropriated; 15% was derived from federal grants, of which more than half was for the school lunch program; 1% was furnished by local governments; and 10% came from other sources. Addition of this large-scale, federally supported, school lunch program since 1940 is chiefly responsible for the interim shift in proportion of federal funds within total state expenditures.

There is wide variation among the states as to their per capita expenditures for health. Tennessee, with a per capita expenditure of $3.26, spent less than any other state in 1950; and Washington, with a per capita cost of $13.58, paid more proportionately than any other of the 48 states. The extensive medical care program in Washington increased expenditures there. In general, states with the lowest income payments in 1949 showed the largest percentage increase since 1940, with respect to both total and per capita expenses for health activities. This is encouraging, since needs are usually greatest in low-income states. Advancement made by these states is due, in part, to the method of allotting federal grants-in-aid: States low in per capita income receive proportionately more for grant programs than do the wealthier states.

It is astonishing to find in each of the survey periods that the state department of health, whose sole function is public health, is responsible for only one-sixth of the aggregate expenditure for this service. Of the total outlay, the department of welfare expends one-fifth, which includes payment, usually to local agencies, for the medical and hospital care of public assistance clients and selected categorical relief groups. The department of education utilizes another tenth, largely for the school lunch program. Approximately one-half of the outlay for health at the state level is spent by special boards and commissions, boards of control, state universities, state hospitals, and other agencies of state government. The relatively insignificant place of the health department in the total expenditure picture may be explained, in part, by the fact that much of the hospital cost, which accounts for approximately 55% of all state level health expenditures, is usually the responsibility of other state agencies.

Because many physicians are chiefly interested in what the health department does, we will now center discussion on that agency. In the fiscal year 1949, the 48 state health departments spent nearly 160 million dollars. State-appropriated funds amounted to more than two-thirds of this total. At the time of the earlier survey, states contributed less than three-fifths of the total. This contradicts the claim sometimes made that federal aid dries up local initiative.

During the 10-year period, total per capita expenditures by state health departments increased by more than 200%, while the increase for the median state amounted to 183%. Roughly, half of the additional outlay might be attributed to rising prices.[3] The remaining half of the expenditure-increase reflects, to a considerable extent, true expansion of program. Items contributing prominently to this growth include, in a number of state health

3. The Department of Commerce estimates an approximate 93% increase occurred in total state and local government costs due to rising prices between 1940 and 1949.

departments, assumption of responsibility for the operation of tuberculosis hospitals and rapid treatment centers; expansion of control programs for tuberculosis, cancer, mental health, and heart disease; extension of organization for local health services; and, in two state health agencies, inauguration of medical care programs.

We see an increase in the delegation of health activities and funds to local areas. This is clear-cut evidence of the dynamic quality of federal-state, state-local relationships. The federal government performs research, formulates standards, and assists the states in establishing and maintaining health programs and facilities. The federal agencies provide assistance to states through grants-in-aid, personnel loans, demonstrations, and advisory and consultative services. The state health agency, in turn, operates in one or a combination of ways. It enforces state laws, promulgates rules and regulations, and renders direct services through staff members of the state central and district offices. It also provides local grants and promotional, supervisory, and consultative services to local health departments.

Personnel counts in health and other agencies are often employed as a rough estimate of service capacity. Full-time staff assigned to state health activities by all agencies of state government has increased by about two-thirds during the decade. Noninstitutional, full-time personnel currently employed by the 48 states for some types of health work number 26,000. There were about 16,000 such employees in 1940. The great majority are employees of the state health departments.

Personnel practices in the various state health agencies have changed over the period. Amendments made in 1939 to the Social Security Act and to the Surgeon General's grant-in-aid regulations have continued to stimulate application of the merit principle in the recruitment and retention of employees. Coverage, however, varies widely from state to state. In 19 states, all or almost all state agencies are included in a single merit system. In some of the remaining states, separate plans are in operation for different agencies; in still others, joint systems include all departments affected by the 1939 amendment. Even wider disparity overspreads the activities of individual merit system units.

Salary scales are usually considered indicative of the progressive nature of an organization. Studies on average annual salaries for health officers and several categories of program directors are available for 1936 [4] and 1951.[5] Comparison of these schedules shows an increase of 109% in salaries of health officers and directors of sanitary engineering, an increase of 107% in remuneration for directors of laboratory services, and a 90% rise in the average annual salary of directors of nursing. However, when considered against an increase of 89% in consumers' prices [6] during essentially the same interval, and rises in tax rates, it seems clear that the salaries of some program heads have merely kept abreast of the cost of living, and others have fallen below that level.

Few will deny that inadequate salary schedules in many areas have caused the dispersion of public health workers to other, more lucrative fields. In addition, the small reserve of trained manpower available in 1940 has been consistently drained by war and postwar activities. During this decade the agencies have been faced with the necessity of developing their own staff members to carry on present functions and to fill higher positions in the department as opportunity arises. Training of public health workers has now become an important part of state health work. The survey shows increasing attention and funds devoted to it. Formal types of training or refresher and intramural courses are offered to some personnel in 49 of the 53 state and territorial jurisdictions.

In 1950, approximately 11,000 persons received training offered by state health departments, as compared to about 850 trainees in 1940. Nurses, physicians, and sanitation personnel, in that order, received most of this training. The emphasis is on short courses, however, because of the heavy work load. Only one-eighth of the training in 1950 was for periods longer than three months. In 1940 more than half of the training was longer than three months.

Thus ends our reporting of the highlights in the 1950 survey. If space permitted, we could give still other and equally impressive examples of development and dispersion in state health programs. What do these diverging trends mean, and where do they lead? It is difficult to escape the conclusion that the desire for health is a compelling urge in American life, but as yet insufficient leadership has emerged around which the separate forces will rally. Possibly the strength of the movement lies in its many sources of origin. Possibly it is too early to channelize this tide, the depth and breadth of which cannot now be measured. We of traditional public health and medical background naturally had hoped that the state health department might be the coordinating, if not the integrating, mechanism in the states, but we fear its current orientation is too narrow.

That which was presented in 1940 as a plea must now be regarded in stronger terms. Today it is even more imperative that maximum efficiency of organization and cohesive action be obtained, if full advantage of all the technical developments currently at our command is to be realized. No matter from whose viewpoint the issue of overlapping health services is approached, from that of the economist, the business man, the administrator, the physician, or the consumer, there is little to recommend it.

For members of the American Medical Association, as a professional medical body interested in the total health of each individual in this country, the trend which has been portrayed here should invite serious reflection. Only by broader orientation of the state health department can the extreme dispersion of health functions be reduced. The medical profession can exert a strong influence toward accomplishing this. With the help of physicians, the hope is still strong that future reports might reveal extraordinary progress toward unification and coordination of all major state public health functions within the principle health agency.

4. From grant-in-aid budgets on file in the State Grants Division, U. S. Public Health Service.

5. Kimble, S. A.: Salaries of State Health Department Personnel, Pub. Health Rep. 67: 26-30 (Jan.) 1952.

6. Consumer Price Index, United States Department of Labor, 1951.

# CLINICAL NOTES

## AGRANULOCYTOSIS FOLLOWING USE OF PHENYLBUTAZONE (BUTAZOLIDIN®)

### REPORT OF A CASE

*Carl Hinz, M.D.*
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*Burton Cominsky, M.D.*
*and*
*Leonard M. Gaines, M.D., New York*

The effectiveness of phenylbutazone (butazolidin,® 3,5-dioxo-1,2-diphenyl-4-n butylpyrazolidin) in the control of pain and inflammation in gout, rheumatoid arthritis and other disorders, has naturally resulted in its rapid acceptance as an anti-inflammatory agent. A number of side-effects resulting from its use have been observed. These include gastric irritation, skin rashes, fever, salt and water retention, and some degree of bone marrow depression. Despite its structural similarity to aminopyrine, no serious agranulocytosis has previously been reported. This complication has been recently observed and constituted the basis for the present case report.

#### REPORT OF CASE

E. S., a 43-year-old single white woman, had been followed at the Presbyterian Hospital since 1944, at which time she had early rheumatoid arthritis of three months' duration. In spite of a variety of therapeutic regimens, the disease continued to be active, and her status had progressed to the category of stage 3, class 3, of the classification of the American Rheumatism Association.[1]

During this period of observation, it is noteworthy that no evidence of toxicity developed in association with several courses of gold administered between 1944 and 1949. Numerous white blood counts were normal. Two brief episodes of epigastric distress during 1951 appeared to be related to acetylsalicylic acid (aspirin) intolerance. A gastrointestinal series during one of these episodes was reported as essentially normal.

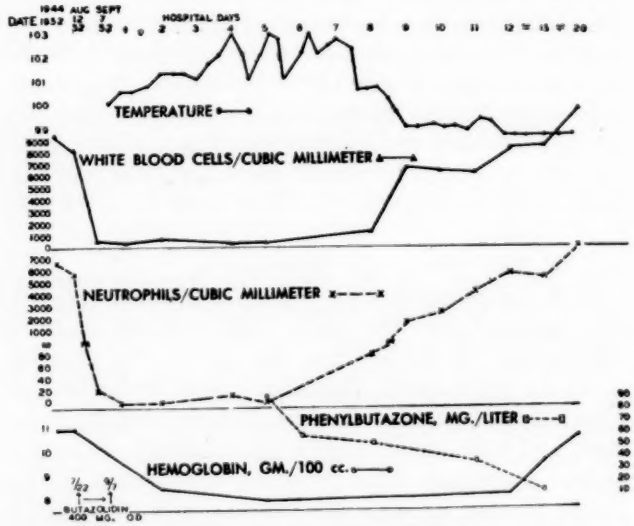
Oral administration of cortisone was begun in September, 1951, on a schedule of 125 mg. daily. By January, 1952, this was gradually reduced to a maintenance dose of 75 mg. supplemented by 2.4 gm. of acetylsalicylic acid per day, but the patient continued to complain of some pain and stiffness of her joints.

Because of increasing subjective complaints and our reluctance to increase the dose of cortisone, 400 mg. of phenylbutazone daily was given orally beginning on July 22, 1952, with the 75 mg. of cortisone. When seen again in the clinic on Aug. 12, the patient was feeling much improved, with marked reduction in pain and stiffness. She had found that she was able to discontinue ingestion of acetylsalicylic acid completely. At this time the hemogram was normal except for a normocytic anemia associated with rheumatoid arthritis (chart).

Forty days after administration of phenylbutazone was started, the patient became aware of a soreness of the mouth and rectum, nausea and vomiting without epigastric distress after eating, and a feeling of weakness and faintness. These symptoms persisted and progressed in intensity. Finally she sought admission to the hospital six days later. It should be noted that up to and during this time she had had greater relief from her arthritic symptoms than for some time past. The phenylbutazone therapy was discontinued when she was admitted. At no time was there exposure to any other known toxic agent.

*Physical Examination.*—The patient appeared pale and acutely ill. The temperature was slightly elevated, 100 F, and the pulse was rapid, 100 per minute. The blood pressure was 105/70. Apart from the stigmas of rheumatoid arthritis, the points of special interest were as follows: The gums were inflamed and hypertrophied and on the hard palate were a number of raised, white lesions covered by a yellow exudate. An enlarged, tender, lymph node was present in the right upper anterior cervical chain. The anal mucosa was inflamed. The skin was pale but free of rash and petechiae.

*Initial Laboratory Results.*—The white blood cell count was 500. A differential count on 50 cells showed 4% polymorphonuclears, 92% lymphocytes, 2% basophils, and 2% myelocytes. The hemoglobin level was 8.4 gm. per 100 cc. (Sahli), with a red blood cell count of 3 million and 0.2% reticulocytes. There were 200,000 platelets. Bone marrow aspiration smears on the second hospital day showed absence of granulocytic forms and decreased erythrocyte formation.




Summary of temperature and laboratory findings during course of agranulocytosis due to phenylbutazone.

Other pertinent findings were a negative direct and indirect Coomb's test, normal mechanical and osmotic fragility tests, a trace of serum bilirubin, a normal fecal urobilinogen level, and negative stool guaiac test. Cultures from the nose and throat showed Staphylococcus aureus hemolyticus, while those from the mouth showed B. alcaligenes. Blood cultures were negative.

*Course.*—During the first seven days of hospitalization, the patient continued to complain of weakness, nausea, vomiting, and soreness of the mouth. A large, punched-out, necrotic ulcer developed in the region of the right tonsillar fossa associated with dysphagia. The temperature during this time varied between 101 and 103 F. On the eighth hospital day, symptomatic improvement began and coincided with a return of the temperature and white blood count toward normal. This improvement continued, but arthritic symptoms of pain and stiffness, which had been of little note during the period of agranulocytosis, reappeared on the 10th hospital day and became the dominant complaint.

*Laboratory Results.*—As can be seen from the chart, the total peripheral white blood cell count was low, with approximately

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Fellow of the Canadian Arthritis and Rheumatism Society (Dr. Lamont-Havers).

Dr. J. J. Burns of the New York University Research Division, Goldwater Memorial Hospital, made the plasma phenylbutazone determinations.

Corticotropin (ACTH) was provided by the Armour Laboratories and the Wilson Laboratories, Chicago. The phenylbutazone (butazolidin®) was supplied by Geigy Pharmaceuticals, New York.

From the Department of Medicine, Columbia University College of Physicians and Surgeons, and the Edward Daniels Faulkner Arthritis Clinic of the Presbyterian Hospital, New York.

This study was aided in part by a grant from the Masonic Foundation for Medical Research and Human Welfare. The cortisone used in this study was supplied in part by Merck & Co., and in part purchased with funds supplied by the United States Public Health Service (grant A-21).

1. Steinbrocker, O.; Traeger, C. H., and Batterman, R. C.: Therapeutic Criteria in Rheumatoid Arthritis, J. A. M. A. **140**: 659-662 (June 25), 1949.

500 cells per cubic millimeter, with few if any neutrophils, for eight days after the drug was discontinued. Recovery began to take place on the eighth hospital day, with a rapid return of the total white blood cell count and differential count to normal levels. The hemoglobin level, which had been consistently about 10.9 gm. per 100 cc., with a red blood count of 4,300,000 before the onset of agranulocytosis, had fallen to 7.9 gm., with a red blood count of 2,340,000 by the fifth hospital day and then slowly rose to 9.5 gm. by the 15th hospital day and 10.5 gm. on the 20th hospital day. The reticulocyte level, as stated, was depressed, being 0.2% on admission. On the ninth hospital day, it had risen to 1.6% and to 2.0% on the 12th hospital day.

Bone marrow aspirations on the 12th hospital day showed marked hyperplasia of the granulocytic series, with only moderate hyperplasia of the erythrocyte elements. There was a slow fall of plasma phenylbutazone levels from 93 mg. per liter on the 5th hospital day to 15 mg. per liter on the 15th hospital day. These days also correspond to the lapse time since ingestion of the last dose of phenylbutazone.

*Treatment.*—Treatment consisted of the continuation of oral administration of cortisone in a dose of 75 mg. daily, and administration of 1,600,000 units of procaine penicillin G (crysticillin®) daily. These were supplemented with corticotropin (acthar®-gel [Armour]), 40 units intramuscularly from the 5th to the 11th day; vitamin $B_{12}$, 10 μg intramuscularly from the 6th to the 13th day; folic acid, 5 mg. from the 3rd to the 13th day; injectable vitamin B (solu-B®), 1 ampul from the 6th to the 13th day; streptomycin, 2 gm. from the 5th to the 13th day; and 500 cc. of blood on the 7th day.

## COMMENT

Phenylbutazone, an effective antiphlogistic pyrazole derivative, has been recently introduced. When phenylbutazone is used with equal parts of aminopyrine ("irgapyrine"), no serious hematological effects and only rare transitory leukopenias have been noted after wide clinical use.[2] In rats, no toxic effects have been noted after 28 days of administration in doses 5 to 10 times as great as those used clinically.[3] In the only reported clinical series in which phenylbutazone has been used alone, two questionably related anemias were observed in 140 patients, one in a patient with gastrointestinal hemorrhage and the other in a patient with leukemia. No effects on granulocytes were noted.[4]

The similarity in chemical structure to aminopyrine, however, has suggested that toxic effects on granulocytes might eventually appear. The toxicity of aminopyrine for granulocytes was unequivocally demonstrated in 1932,[5] 30 years after introduction of the drug. The incidence of agranulocytosis due to aminopyrine has been reported at from 0.02% to 1.0%.[6]

In the present patient, agranulocytosis occurred concurrently with administration of phenylbutazone. The only other drug that she received prior to her illness was cortisone, which has not been reported to cause agranulocytosis, and she had not been exposed to known extrinsic toxins.

The symptoms on admission, physical findings, and the almost complete absence of granulocytes in peripheral blood and bone marrow were similar to the findings in the reported cases of acute agranulocytic angina (Schultz's syndrome)[7] due to aminopyrine. The reappearance of granulocytes in marrow and blood coincided with clinical improvement, occurring two weeks after onset of symptoms and at a time when phenylbutazone was still present in small amounts in the blood.

The increasing severity of her preexisting anemia, coincident with the agranulocytosis, followed by a return toward normal with recovery, suggests that the drug may have affected erythrocytes as well, in contrast with the blood dyscrasia induced by aminopyrine. There was no evidence of hemolysis or blood loss, and the change in hemoglobin was not related to fluid retention, which has been observed with administration of phenylbutazone.[2] On admission, there were anemia, a reticulocyte count of 0.2%, and a diminution in the erythrotic marrow elements; with recovery there was a return of reticulocytes to 2%, despite transfusion, and a gradual rise in hemoglobin, which continued beyond the time when a transfusion change is ordinarily manifest. These data suggest that the effect of the drug caused aplasia of erythrocytes as well as of granulocytes without modification of the blood platelets.

It was not thought wise to challenge the patient with a test dose of drug to prove a causal relationship because of reported severe and prolonged reactions to challenging doses of aminopyrine.[8] The role in recovery, if any, of the supplementary drugs given, such as cortisone, corticotropin, liver, folic acid, and vitamin B complex, cannot be assessed.

## SUMMARY

A case of severe agranulocytosis that was apparently due to phenylbutazone (butazolidin®) is reported. Recovery occurred while the drug was still demonstrable in the blood in low concentration. The occurrence of anemia is noted, in contrast to the findings in agranulocytosis due to aminopyrine ("irgapyrine").

## ADDENDUM

Since this report was submitted for publication, four other instances of agranulocytosis following use of phenylbutazone have been recorded, with recovery occurring in all cases.[9]

620 W. 168th St. (Dr. Hinz).

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3. Wilhelmi, G.: The Pharmacologic Properties of Irgapyrin, A New Compound of the Pyrazol Series, Schweiz. med. Wchnschr. **79**: 577-582, 1949.

4. Kuzell, W. C.; Schaffarzick, R. W.; Brown, B., and Marble, E. A.: Phenylbutazone (Butazolidin®) in Rheumatoid Arthritis and Gout, J. A. M. A. **149**: 729-734 (June 21) 1952.

5. Kracke, R. R.: Experimental Production of Agranulocytosis, Am. J. Clin. Path. **2**: 11-30, 1932. Madison, F. W., and Squier, T. L.: Primary Granulocytopenia after the Administration of Benzene Chain Derivatives, J. A. M. A. **101**: 2076-2077 (Dec. 23) 1933.

6. Friese, W.: Agranulocytose nach intravenösen Pyramidongaben, Med. Klin. **45**: 404-405, 1950. Rawls, W. B.: The Effect of Amidopyrin upon the Red, White, and Polymorphonuclear Blood Cells of a Series of 100 Patients, Am. J. M. Sc. **192**: 175-179, 1936.

7. Schultz, W.: Ueber Eigenartige Halserkrankungen, Deutsche med. Wchnschr. **48**: 1495-1497, 1922.

8. Dameshek, W., and Colmes, A.: The Effect of Drugs in the Production of Agranulocytosis with Particular Reference to Amidopyrine Sensitivity, J. Clin. Investigation **15**: 85-97, 1936.

9. Kuzell, W. C., and Schaffarzick, R. W.: Phenylbutazone (Butazolidin®), Bull. on Rheumat. Dis. **3**: 23, 1952.

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**Visceral Pain Referred to Shoulder.**—Three conditions commonly found produce shoulder pain. Diaphragmatic pleurisy and gallbladder disease through irritation of the phrenic nerve may cause pain in the right shoulder. The referred pain of angina pectoris is usually felt in the left shoulder, extending down to the left hand. Occasionally the right side is involved. The associated symptoms and signs of both these conditions are usually sufficiently obvious to leave little doubt as to the diagnosis. The shoulder-hand syndrome is not a complication of angina pectoris, but of myocardial infarction.—S. Nelson, M.D., The Painful Shoulder, *Medical Journal of Australia*, Aug. 30, 1952.

## GONGYLONEMA INFECTION IN SOUTH CAROLINA

### REPORT OF A CASE

*Martin D. Young, Sc.D., Columbia, S. C.*
*and*
*Isaac Hayne, M.D., Congaree-Eastover, S. C.*

The parasitism of man by the nematode Gongylonema is rarely reported. In 1951, Craig and Faust [1] listed 14 cases. Since then, the 15th case has been reported.[2] Seven of these originated in this country, one each from Florida, Georgia, Alabama, Louisiana, and Arkansas, and two from Virginia.[1] Following is the report of a case in which, in 1945, an immature female Gongylonema was removed from the mouth of a Negro woman living in Congaree, S. C.

#### REPORT OF A CASE

The host was a Negro woman, 26 years of age, in good physical condition, who was employed in a laundry. About 9 o'clock one night the patient felt with her tongue a foreign body under the mucosa of her upper lip near the junction with the upper gum. By the following morning the object had moved to the middle of the cheek about half the distance from the mouth to the posterior part of the jaw. She examined this area with a mirror and saw a white coiled worm just under the surface of the mucosa. She went to a physician, but he could find no trace of the worm. Later that afternoon she again felt the worm, this time at the top of the lower lip. It felt to her as if the worm were emerging. At about 5 p. m. she came to one of us (I. H.). The worm was easily seen and apparently was in the process of emerging from the mucosa. It was extracted by grasping the free end with splinter forceps and exerting gentle traction. The worm was removed easily without pain or discomfort. After extraction the worm was exceedingly active, exhibiting a writhing motion and flexing upon itself. This activity continued until the worm was immersed in rubbing alcohol. The subsequent history of the patient was uneventful.

The active migration of the worm is of interest. From the center of the upper lip it migrated half the length of the right cheek and then back again to the center of the lower lip in a period of 20 hours. The worm was threadlike and white in appearance. Its greatest width was 0.18 mm. In handling, the worm was broken into several pieces. An approximation of the length was 17 mm.

The normal definitive hosts of Gongylonema are ruminants, monkeys, swine, and other animals. The eggs of the parasite are ingested by dung beetles and cockroaches, in which some development occurs. The definitive host acquires the infection by eating the parasitized intermediate host. Man is an accidental host, obtaining the infection by food or drink into which the intermediate host has fallen.

The route by which the worm infected this patient is unknown. She lived on a farm and obtained drinking water from a dug well, about 20 feet deep, by the use of wooden buckets and a rope. The well housing was not tightly constructed, so that it would be easy for insects to fall into the water. The barnyard was about 100 feet from the house, and the well was situated about half-way between. Cockroaches were fairly common around the house. While it is possible that she could have obtained the infection by other means, the most obvious source appears to be contaminated well water.

Dr. W. W. Cort, Johns Hopkins University, and Mr. John T. Lucker, Bureau of Animal Industry, U. S. Department of Agriculture, examined this specimen, and both identified the worm as Gongylonema. Mr. Lucker believes that the present specimen is Gongylonema pulchrum.

#### SUMMARY

An immature specimen of the nematode Gongylonema (probably Gongylonema pulchrum) was found in the lip mucosa of a Negro woman in South Carolina. It appears that the most likely source of infection was well water contaminated by an intermediate vector. This apparently is the first reported case of human infection by this parasite from South Carolina and the eighth from the United States.

P. O. Box 717 (Dr. Young).

From the Federal Security Agency, Public Health Service, National Institutes of Health, National Microbiological Institute, Laboratory of Tropical Diseases (Dr. Young), and Congaree Clinic (Dr. Hayne).

1. Craig, C. F., and Faust, E. C.: Clinical Parasitology, ed. 5, Philadelphia, Lea & Febiger, 1951, p. 393.

2. Gaud, J., and Chabaud, A. G.: Présence du nématode Gongylonema pulchrum chez l'homme, au Maroc, Bull. Soc. path. exot. 44: 62-65, 1951.

## SPECIAL ARTICLE

## CONTROL OF U. S. P. ANTI-ANEMIA PREPARATIONS

### SPECIAL REPORT OF THE UNITED STATES PHARMACOPEIA ANTI-ANEMIA PREPARATIONS ADVISORY BOARD

*Robert W. Heinle, M.D., Cleveland*
*Frank H. Bethell, M.D., Ann Arbor Mich.*
*William B. Castle, M.D., Boston*
*Irving M. London, M.D., New York*
*and*
*William T. Salter, M.D., Boston*

NOTE.—*Since 1950 the United States Pharmacopeia Anti-Anemia Preparations Advisory Board has consisted of Drs. Robert W. Heinle, chairman, Irving M. London, secretary, and Frank H. Bethell, William B. Castle, and William T. Salter, members. Dr. Salter's death on July 30 and Dr. Heinle's recent resignation reduced the membership to three. Former members were Drs. C. W. Edmunds (1936-1941), Raphael Isaacs (1936-1942), George R. Minot (1936-1948), Walter W. Palmer (1936-1948), Randolph West (1948-1949), and Maxwell M. Wintrobe (1942-1949).*—ED.

The United States Pharmacopeia Anti-Anemia Preparations Advisory Board was authorized by the U. S. P. Convention and became official under the Eleventh Decennial Revision on June 1, 1936. This Board, composed of five members and originally under the chairmanship of the late Dr. C. W. Edmunds of Ann Arbor, was set up to effect some degree of standardization of liver, stomach, and other preparations designed for the treatment of pernicious anemia. The practical need for this control arose from the fact that at that time no method except study of their clinical effectiveness existed for determining the amount of the then unknown anti-

Because of space limitations, some of the bibliographic references have been omitted from THE JOURNAL and will appear in the authors' reprints.

anemic principle or principles contained in products used for the treatment of pernicious and other nutritional macrocytic anemias. During the decade following the discovery of the value of liver therapy in pernicious anemia in 1926, the pharmaceutical industry developed active preparations of liver and of stomach for oral use and by 1936 had achieved relatively purified and concentrated extracts of liver for intramuscular injection. Consequently, as was stated in the first [1] of the six announcements that the board has published, "because of the variation in the efficiency of different processes of manufacture, the therapeutic activity of the final product does not necessarily correspond to the amount of liver from which it is derived."

In order to provide the medical profession with preparations of known therapeutic potency, it was, therefore, necessary to test the clinical effectiveness of the final manufactured product in the actual treatment of pernicious anemia patients. For this purpose appropriately controlled clinical procedures were prescribed.[2] By means of observations on at least three patients, the amount of each product was determined that would produce specified reticulocyte and red cell responses as well as satisfactory clinical improvement when given in uniform daily amounts.[3] This daily amount of material was defined by the board as a U. S. P. unit and, depending on the route of administration, as either oral or injectable. For the guidance of the profession, the amount of the particular product constituting a U. S. P. unit was stated in the labeling of the product. With the excellent cooperation of the pharmaceutical industry the requisite large number of laborious clinical tests was carried out over a period of years. For all approved products, the reliability at least of a particular manufacturing process invariably employed was demonstrated, and for many products the results of subsequent clinical assays of individual lots made by this process were also analyzed. Evidence of the board's careful attention to detail was seen in its concern over the adequacy of the facilities for firms to repackage liver solutions received in bulk from primary suppliers, a hazardous process at best from a bacteriological standpoint, but one that was practiced very extensively in the pharmaceutical industry. Eventually, hundreds of products and their labels were approved for distribution. From time to time, the names of the manufacturers and the description of their accepted products were published in the pharmaceutical literature. In these announcements [4] the regulations and standards of the board were also set forth. These, of course, applied only to official U. S. P. preparations and not to proprietary mixtures, even when they contained liver or stomach preparations. Liver with stomach U. S. P., although a mixture, was not so regarded "because the mutually potentiating therapeutic activity of its components is directed towards the same nutritional deficiency." [4b] This view is now supported by clinical evidence demonstrating the enhanced absorption of vitamin $B_{12}$ accountable to the "intrinsic factor" present in such preparations.[5]

By 1938, the best interests of the medical profession and of the manufacturers appeared to indicate that the concentration of liver injection U. S. P. should be limited to 15 U. S. P. units or less.[2] Recently, in order to avoid a needless variety of concentrations that were often merely dilutions of greater concentrations, the board recommended that only preparations containing either 10 or 15 U. S. P. units (injectable) per cubic centimeter be included in the latest revision of the Pharmacopeia. Liver injection (crude) U. S. P. became official in 1944, and with the thirteenth revision in 1947 the strength of this product was restricted to either 1 or 2 U. S. P. units (injectable) per cubic centimeter. This change was recommended by the board because of the lack of convincing evidence that this preparation, although derived directly from an early extraction stage involving 70% alcohol by volume, contained active principles in clinically effective amounts other than those present in the supposedly more refined liver injection U. S. P.

Present evidence indicates that the therapeutic activity of both types of liver injection in pernicious anemia is almost, if not entirely, due to their content of vitamin $B_{12}$. The potency of powdered stomach U. S. P. and of liver with stomach U. S. P. derives mainly from the presence of both vitamin $B_{12}$ and of the so-called "intrinsic factor." The U. S. Pharmacopeia XIV includes these preparations as well as dry and liquid liver extract U. S. P. for oral use. However, these liver extracts, even in the considerable amounts required for oral use, are of particular value [6] only in the relatively uncommon instances of macrocytic anemia with megaloblastic bone marrow (Wills' factor deficiency) developing in infants and children [7] or during pregnancy.[8] Such patients are found to be refractory to liver injection U. S. P. or to vitamin $B_{12}$ injection U. S. P.[9] At least some of these relatively crude liver preparations for oral use contain, in addition to vitamin $B_{12}$, sufficient amounts of folic acid or of the so-called citrovorum factor as probably to account for their effectiveness in such patients. These anemias will respond to folic acid U. S. P.[10] or to its metabolically active form, citrovorum factor or folinic acid [11] as such.

In 1945 folic acid in the form of synthetic pteroylglutamic acid became available to the medical profession as the first pure substance capable of evoking a hematological response in pernicious and related macrocytic anemias. As this is a recognized chemical entity subject to easily defined biochemical or biological control, the sat-

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1. Report on Potency of Liver Products by United States Pharmacopeia Anti-Anemia Preparations Advisory Board, J. A. M. A. **110**: 812 (March 12) 1938.

2. U. S. P. Anti-Anemia Preparations Advisory Board: Second Announcement of U. S. P. Anti-Anemia Advisory Board, J. Am. Pharm. A. **27**: 629 (August) 1938.

3. U. S. P. Anti-Anemia Preparations Advisory Board, Third Announcement: Criteria Used by United States Pharmacopeia Anti-Anemia Preparations Advisory Board in Assigning Unitage to Anti-Anemia Preparations, J. Am. Pharm. A. (Prac. Ed.) **1**: 53 (Feb.) 1940. Fourth Announcement, U. S. P. Anti-Anemia Preparations Advisory Board: Additional Products to which U. S. P. Anti-Anemia Unit Value Has Been Assigned, ibid. **4**: 122 (April) 1943.

4a. Footnotes 1, 2, 3, and 4.

4b. Fifth Announcement of the U. S. P. Anti-Anemia Preparations Advisory Board: Statement of Board, J. Am. Pharm. A. (Prac. Ed.) **9**: 660 (Nov.) 1948.

4c. Sixth Announcement of the U. S. P. Anti-Anemia Preparations Advisory Board, Drug Standards **20**: 156 (July-August) 1952.

5c. Welch, A. D.; Scharf, V.; Heinle, R. W., and Meacham, G. C.: Assay for Intrinsic Factor in Patients with Pernicious Anemia in Remission Given Radioactive Vitamin $B_{12}$, Proc. Fed. Am. Soc. Exper. Biol. **11**: 308 (March) 1952.

6. Watson, J., and Castle, W. B.: Nutritional Macrocytic Anemia, Especially in Pregnancy: Response to a Substance in Liver Other than that Effective in Pernicious Anemia, Am. J. M. Sc. **211**: 513 (May) 1946.

9. Day, L. A.; Hall, B. E., and Pease, G. L.: Macrocytic Anemia of Pregnancy Refractory to Vitamin $B_{12}$ Therapy; Response to Treatment with Folic Acid: Report of Case, Proc. Staff. Meet., Mayo Clin. **24**: 149 (March 30) 1949.

isfactory use of this substance required no more information for the guidance of the physician than a statement of the amount of the compound present whether in pure form or in a mixture. Consequently, it was unnecessary for the board to undertake the clinical testing of the anti-anemic activity of folic acid U. S. P.[4f] the regulation of which, like other official preparations of vitamins, depended on the recommendations of the U.S.P. Vitamin Advisory Board. Moreover, folic acid was subsequently shown to be inadequate for control of either the hematological or neurological lesions of pernicious anemia, although it is fully effective in certain other macrocytic anemias.

Shortly after the isolation of vitamin $B_{12}$ and the demonstration of its effectiveness in the treatment of pernicious anemia in 1948, appropriate spectrochemical methods of assay, at least for relatively concentrated solutions, were developed. Consequently, the problem of the clinical testing of the hematopoietic activity of vitamin $B_{12}$ injection U.S.P. was also rendered unnecessary. In 1950, after more sensitive microbial methods had been described, a collaborative study of the vitamin $B_{12}$ activity of liver injection U.S.P. was set up under the auspices of a special Pharmacopeia study panel, which included representatives from the vitamin and anti-anemia preparations advisory boards. With the active technical participation of members of the pharmaceutical industry, a satisfactory microbial assay method was evolved and was shown to be applicable both to liver injection and to liver injection (crude) U.S.P. Thereupon, it was demonstrated that despite every effort on the part of manufacturers, considerable variation existed in the actual content of vitamin $B_{12}$ activity of products with similar U.S.P. unitage. In view of the inherent difficulties of clinical testing, including the long recognized and considerable variability of the responses of different patients even to identical preparations of liver injection U.S.P., it became clear that the medical profession would be more satisfactorily guided in its use of liver injection by a statement of a product's vitamin $B_{12}$ activity than of its U.S.P. unitage.[4c] For these reasons the board has not attempted to establish a factor for converting U.S.P. units into microgram equivalents of vitamin $B_{12}$ activity. In considering dosage, however, the physician may for convenience and with sufficient accuracy for clinical purposes equate the former U.S.P. units (injectable) with micrograms of vitamin $B_{12}$ given by injection. This requires essentially no change in the volume of the usual dose of the injectable preparations.

The board considers that liver injection U.S.P. and liver injection (crude) U.S.P. are, so far as the treatment of pernicious anemia is concerned, solutions of vitamin $B_{12}$. Liver injection U.S.P. containing 20 $\mu$g of vitamin $B_{12}$ activity per cubic centimeter is considered to be fully as active as that formerly labeled as containing 15 U.S.P. units (injectable) per cubic centimeter.[4c] As a result of the recommendations of the board, the Third U.S.P. XIV Supplement, which became official on Jan. 1, 1952, provides that the labeling of liver injection and of liver injection (crude) U.S.P. shall no longer indicate their content of U.S.P. units, but only their vitamin $B_{12}$ activity as determined by the official microbial procedure. The supplement designates as official for parenteral use only liver injection containing the equivalent of either 10 or 20 $\mu$g of cyanocobalamin (vitamin $B_{12}$) activity per cubic centimeter and liver injection (crude) containing vitamin $B_{12}$ activity equivalent to either 1 or 2 $\mu$g of cyanocobalamin per cubic centimeter. For the official assay a U.S.P. cyanocobalamin reference standard is specified.

Vitamin $B_{12}$, like purified liver extracts, when given by injection in pernicious anemia, is usually many (perhaps 60 to 100) times as active as when given by mouth. Thus, patients who respond maximally to the daily intramuscular injection of 1 $\mu$g of vitamin $B_{12}$ may respond but weakly to the daily administration by mouth of 50 or even 100 $\mu$g of vitamin $B_{12}$.[12] This is apparently due to the severely limited and unpredictable ability of the patient with pernicious anemia to absorb even as little as 1 $\mu$g of vitamin $B_{12}$ a day from the alimentary tract. This striking and specific failure of assimilation is in turn the result of the lack in pernicious anemia of the so-called "intrinsic factor," which is present in the gastric juice of normal individuals.[12b] A limited absorption of vitamin $B_{12}$ is found with all preparations of liver for oral use. Even when the absorption of vitamin $B_{12}$ is facilitated by the presence of intrinsic factor, as in powdered stomach U.S.P. or in liver with stomach U.S.P., the hematopoietic activity of the vitamin $B_{12}$ present does not approach that of the same amount of vitamin $B_{12}$ administered by parenteral injection. Consequently, there seems to be no present possibility of substituting an assay for vitamin $B_{12}$ for the existing methods of clinical testing in the case of these oral preparations. For this reason the board continues to require clinical tests of hematopoietic and clinical activity and appropriate labeling in terms of U.S.P. units (oral) for all official preparations of liver and/or stomach for oral use.[4c] Whether the present availability of chemically pure vitamin $B_{12}$, folic acid, and citrovorum factor will render these earlier preparations unnecessary in the treatment of pernicious and other nutritional macrocytic anemias remains to be seen.

To date, no significant difference has been detected between the effects of adequate amounts of liver injection U.S.P. and of vitamin $B_{12}$ injection U.S.P. in the treatment of any aspect of pernicious anemia. With either, prompt initial subjective improvement appears and is then followed by the now classical hematopoietic responses and the arrest of gastrointestinal and neural manifestations. Although informed opinions differ somewhat, the maintenance treatment of uncomplicated cases of pernicious anemia is apparently satisfactorily achieved by the injection at intervals of not longer than a month of either of these preparations in such an amount that the patient will receive an average of at least 1 $\mu$g of vitamin $B_{12}$ per day.[13] Because such relatively infrequent injections appear to be entirely satisfactory, the much greater frequency of treatment required with the use of liver injection (crude) U.S.P. constitutes an undesirable and unnecessary inconvenience for patient and physician and should logically lead to the abolition of this preparation. Although, after a single injection of more than

12a. Meyer, L. M., and others: Oral Treatment of Pernicious Anemia with Vitamin $B_{12}$, Am. J. M. Sc. **220**: 604 (Dec.) 1950.

12b. Hall, B. E.: Studies on the Nature of the Intrinsic Factor of Castle, Brit. M. J. **2**: 585 (Sept. 9) 1950.

25 μg, much of the vitamin $B_{12}$ is promptly lost in the urine,[14] enough for clinical purposes appears to be retained in the body when, for example, 30 μg are given once a month. On the other hand, because of the large urinary loss, and because it has been shown [15] that relapse on discontinuance of treatment is not delayed by the injection of even large amounts of liver extract, there would appear to be no advantage in producing liver injection U.S.P. (or vitamin $B_{12}$ injection U.S.P.) containing more than 20 μg of vitamin $B_{12}$ activity per cubic centimeter. Indeed, the production of solutions containing higher concentrations of vitamin $B_{12}$ from liver may be difficult and unduly expensive to manufacture; and their parenteral use, as with higher concentrations of vitamin $B_{12}$ injection, is wasteful, renders accurate dosage difficult, and has no convincingly demonstrated clinical advantage in the treatment of pernicious anemia.

622 W. 168th St. (Dr. London).

14. Conley, C. L., and others: Observations on the Absorption, Utilization, and Excretion of Vitamin $B_{12}$, J. Lab. & Clin. Med. **38**: 84 (July) 1951.

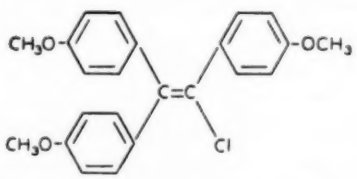
# COUNCIL ON PHARMACY AND CHEMISTRY

## NEW AND NONOFFICIAL REMEDIES

*The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.*

R. T. STORMONT, M.D., *Secretary.*

**Chlorotrianisene.**—TACE (Merrell).—Chlorotris(*p*-methoxyphenyl)ethylene.—Tri-*p*-anisylchloroethylene.—$C_{23}H_{21}ClO_3$.—M.W. 380.86.—The structural formula of chlorotrianisene may be represented as follows:




*Actions and Uses.*—Chlorotrianisene in general shares the actions and uses of the estrogens (see general statement on estrogens). However, it possesses certain peculiar attributes not common to other estrogens. When administered orally, the amount of estrogenic activity recovered in the stool exceeds the amount originally administered in the form of chlorotrianisene. This indicates that by some metabolic process the potency of the drug is enhanced. A hint at the probable locale of this enhancement is furnished by experiments in which the activity of chlorotrianisene is increased by incubation with liver homogenates. Chlorotrianisene, in the dosages used in experimental studies on laboratory animals, apparently induced less pituitary or adrenal hyperplasia than other estrogens. The compound is stored in the body fat from which it is slowly released over a period of time, varying with the amount administered. Therefore, its action will persist for varying periods following discontinuance of the drug. Its use in high dosages in mammary cancer occurring five years or more past the menopause is not recommended because of uterine bleeding, although there is less tendency toward withdrawal bleeding in the lower dosage recommended for the menopause.

*Dosage.*—Chlorotrianisene has a lower milligram equivalent than other synthetic estrogens and doses are higher for comparable effects. The average dose for relief of menopausal symptoms varies between 12 and 24 mg. daily by mouth. In prostatic cancer, 24 mg. daily has proved effective in relieving symptoms.

*Tests and Standards.*—

*Physical Properties:* Chlorotrianisene is a white, odorless, crystalline powder, m. p. 114-117° (becomes syrupy at about 108°). It is freely soluble in acetone, benzene, and chloroform; and very slightly soluble in water. The amounts which dissolve in the following solvents to form 100 ml. of solution are: 0.28 gm. in alcohol and 3.6 gm. in ether.

*Identity Tests:* Dissolve about 10 mg. of chlorotrianisene in 2 ml. of sulfuric acid: a very dark purple solution forms *(distinction from diethylstilbestrol and mestibol, which give an orange color; from hexestrol, which gives no color; from benzestrol, which gives a yellow color; and from promethestrol dipropionate, which gives an orange-red color).* Dilute with 5 ml. of water: the color rapidly changes from dark purple to pink and the solution finally becomes turbid.

A 0.001% solution, prepared as described in the spectrophotometric assay for chlorotrianisene, exhibits an ultraviolet absorption minimum at about 278 mμ and a maximum at about 310 mμ [specific absorbancy, E(1%, 1 cm.), about 423].

*Purity Tests:* Dry about 1 gm. of chlorotrianisene, accurately weighed, in a desiccator over sulfuric acid for 24 hours: the loss in weight does not exceed 1.0%.

Char about 1 gm. of chlorotrianisene, accurately weighed, cool the residue, add 1 ml. of sulfuric acid, heat cautiously until evolution of sulfur trioxide ceases, ignite, cool, and weigh: the residue does not exceed 0.05%.

*Assay:* (Chlorotrianisene) Prepare a 0.001% solution of chlorotrianisene as follows. Transfer to a 100 ml. volumetric flask 0.1 gm. of chlorotrianisene, accurately weighed, fill to the mark with chloroform, and mix. Transfer to a second 100 ml. flask 10 ml. of this solution, fill to the mark with chloroform, and mix. Transfer to a third 100 ml. flask 10 ml. of this last solution, fill to the mark with chloroform and mix. Determine the absorbancy in a 1 cm. quartz cell at 310 mμ, using chloroform as a blank. The concentration of chlorotrianisene in the solution in mg./ml. = absorbancy ÷ 42.3. The amount of chlorotrianisene is not less than 95.0 nor more than 105.0%.

(Chlorine) Transfer about 0.5 gm. of chlorotrianisene, accurately weighed, to a 100 ml. round-bottomed flask with a ground glass joint. Add 15 ml. of absolute alcohol and connect the flask to a reflux condenser. Heat gently with a small flame. When the chlorotrianisene dissolves and the alcohol boils add, through the condenser, 1.5-2.0 gm. of clean sodium in small pieces (add all of the sodium at once). Reflux the solution for 1 hour. There must be free sodium present during this entire period. Shake the flask frequently, and if a solid forms, add small quantities (5 ml.) of absolute alcohol with shaking until the solid goes back into solution. After 1 hour of refluxing and while the solution is still boiling, add absolute alcohol to destroy the excess sodium. Heat for 15 min. after the last trace of sodium disappears. Wash the condenser with a small amount of water, disconnect the flask, and transfer the contents quantitatively to a 250 ml. beaker. Cool the solution and acidify with nitric acid (10-15 ml.). Add exactly 25 ml. of 0.1 *N* silver nitrate, allow the precipitate to settle, filter, and wash with water. Collect the filtrate in a 250 ml. Erlenmeyer flask. Add 2 ml. of ferric ammonium sulfate T.S. and titrate the excess silver nitrate with 0.1 *N* ammonium thiocyanate. Each milliliter of 0.1 *N* silver nitrate consumed is equivalent to 0.003546 gm. of chlorine and 0.03809 gm. of chlorotrianisene. The amount of chlorine is not less than 8.94 nor more than 9.68%, equivalent to not less than 96.0 nor more than 104.0% of chlorotrianisene.

**Dosage Forms of Chlorotrianisene**

CAPSULES. *Assay:* Accurately weigh not less than 10 capsules. Cut the capsules open and drain the oil into a 50 ml. beaker. Wash the empty capsules thoroughly with ether, drain, and air dry. Weigh the dried capsules and calculate the weight of the contents. Determine the density of the oil and calculate the volume of the contents per capsule. Transfer exactly 2 ml. of the oil from the capsules to a 100 ml. volumetric flask, fill to the mark with chloroform, and mix. Transfer to a 50 ml. volumetric flask 2 ml. of this solution, fill to the mark with chloroform, and mix. Determine the absorbancy in a 1 cm. quartz cell at 310 mμ, using a like concentration of the solvent oil in chloroform as a blank. The concentration of chlorotrianisene in the solution in mg./ml. = absorbancy ÷ 42.3. The amount of chlorotrianisene is not less than 92.5 nor more than 107.5% of the labeled amount.

The Wm. S. Merrell Company, Cincinnati.

*Capsules TACE:* 12 mg. in corn oil. U. S. patent 2,430,891.

**Sodium Acetrizoate** (See New and Nonofficial Remedies 1952, p. 283).

Mallinckrodt Chemical Works, St. Louis.

*Solution Urokon Sodium 70%:* 25 cc. ampuls and 50 cc. vials. A solution containing 0.7 gm. of sodium acetrizoate in each cubic centimeter. Stabilized with 0.12 mg. of calcium ethylenediaminetetraacetate and buffered with 0.15 mg. of sodium biphosphate in each cubic centimeter. U. S. trademark 519,732.

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## CLINICAL IMPRESSION AND CLINICAL INVESTIGATION

### GUEST EDITORIAL

*Henry K. Beecher, M.D., Boston*

*"I have used the remedy you sent me in several patients. It is my distinct impression that this is the finest thing ever made for the purpose."*—Statement by an Eminent Clinician.

Special problems in every field of learning have to be identified before they can be solved. In clinical investigation this tiresome truism has not been given the attention it deserves. Clinical investigation is often derived from—and as often destroyed by—clinical impression. In the strengths and often unconsidered weaknesses of clinical impression there is a significant problem.

Very likely a better title for this brief comment would be "Clinical Impression and the Notebook and Pencil." But such a title might perhaps overemphasize tools. That would be unwise, for sound clinical impression comes in large part from observation, one of the principal sources of knowledge. There are only two others: experimentation and reasoning. Clinical impression is often derived from the first of these alone, and unfortunately sometimes from less. Lacking as we do perfect memories, the fruits of the great sources of knowledge quickly spoil unless they are preserved, so in the growth of knowledge, recording (the notebook and pencil) takes rank as a principal aid to the advance of learning. Careful recording emerges as the indispensable preservative and protector of accurate clinical impression. Information, however derived, requires a record if it is to live, a notebook and pencil, so to speak. These simple tools are a neglected instrument. Some fields require abstruse recording devices; the clinician is lucky in that his chief need is a notebook and pencil. It is a pity he sometimes uses them so little.

In the welter of scientific paraphernalia, the mass spectrographs, the Geiger counters, the tagged atoms and the marked molecules, the importance of the lowly notebook and pencil is sometimes forgotten by the clinical observer. Judging by the flood of applications for funds that today pour into Washington, even the newest investigator does not seem to think he can function unless he has one or more complex (and expensive) instruments. The whole crazy, upside-down situation was illustrated the other day in a short letter that said, "Dear doctor, I have bought an oximeter. Will you suggest a research problem to use it on?" There is the belief that discovery is a matter of machinery. It is just possible, however, that there is still a place in clinical investigation for the great idea preserved, protected, and developed with no more physical tools than the notebook and pencil.

Observation that leads to clinical impression is a primary source of information; but conclusions based on clinical impression are subject to threats of several kinds. Clinical impression, unaided and undisciplined by painstaking recording, can be a treacherous guide. One can ask, what else threatens clinical impression as a basis for sound judgment? Here are a few such threats. A frequent source of error in clinical appraisal is the poorly designed experiment. For example, there is common failure to appreciate the effectiveness of placebos in treating certain ills. Even in a group of patients in severe, steady, postoperative pain, a third will have their pain relieved by a placebo. This sizable percentage is what has allowed many an erroneous statement concerning the pain-relieving power of a given agent to get by. Many an honest man has extolled this or that as effective when all the power it had was as a placebo. Recognition of the high effectiveness of placebos in treating subjective ailments is a first safeguard against extravagant statement.

There are other kinds of threats; for instance, we had better admit that there is some truth in Rousseau's depressing statement: "The wise man doesn't exist who fails to prefer the lie invented by himself to the truth discovered by another." In this frailty there is immodesty (the affectation of infallibility), superficial observation, and too little observation; there is ignorance, stupidity, too much respect for tradition, inability to reason, laziness as a bar to reasoning, and hasty conclusion, to name a few defects. These are the source of bias. Bias is the greatest threat to sound judgment.

In the natural sciences of mathematics, physics, and chemistry, facts newly discovered are subject to forthright check in objective terms. It is often different with biological phenomena, especially those newly found in man. Phenomena demonstrated in the clinic are subject to a curious trial-by-bias. This must always be so as long as casual clinical impression is allowed to maintain the high authority it claims. Unfortunately, clinical impression represents, to the man of short memory, the last two or three cases he has seen. To the man of longer memory, bias can still distort fact. Clinical impression provides, to lift Cajal's phrase, "doctrine maintained exclusively by the principal of authority." The bias that destroys what might have been good clinical impression is a defect of the spirit, just as is over-reverence for authority.

Accurate clinical judgment is difficult enough when objective matters are under consideration. There is the elderly clinician who can "smell" typhoid fever, "feel" cancer, "taste" diabetes, "see" tertiary syphilis without outward sign, and "hear" pneumonia across the room, and who explains on being questioned that he does it in the same way you recognize your grandmother. All credit should be given to these keen observers. Observation is difficult enough when objective signs are under consideration; it is more difficult when subjective responses are examined. Then not only is the patient's sending station of doubtful accuracy but the observer's reception

of the signals is confused by extraneous noises produced by tradition, by confusion derived from his own more or less acute perception, by his failure to seek patiently for the truth, but most of all by bias.

The man of good will is foolish indeed if he thinks he has escaped or can escape bias simply because his heart is right. Regard for revered teachers and respected friends and for one's own honest observations leads, sometimes, to major error. The wise man actively eliminates bias: He protects himself with the stalwart supports of the "unknowns" technique in which placebos are inserted, with "randomization" of the agents tested, with the necessary masses of data, but above all with the use of a notebook and pencil.

Bias and most of the other frailties that weaken clinical impression as a source of information are defects of the spirit, but, as Payot believed, the spirit as well as the intelligence can be educated. Clinical investigation cannot be strong while bias persists. It cannot be strong while unsound clinical impression has authority.

## CARBON TETRACHLORIDE POISONING

Attention has recently been directed to carbon tetrachloride as a source of potential poisoning in daily life. Carbon tetrachloride is used widely in industry and by the general public as a noninflammable dry-cleaning agent and as a fire extinguisher under many trade names; it is also used as a degreaser for metal parts; as a solvent for crude rubber, tars, and resins; as a delousing agent, a dry-hair shampoo, and an anthelmintic; and in the fumigation of grain. According to Myatt and Salmons,[1] carbon tetrachloride poisoning is frequently unrecognized, being erroneously treated as nephritis, heart disease, or hepatitis. The toxicity of the agent is enhanced in alcoholics and in malnourished persons. Almost all 15 cases of poisoning reported by the authors involved either persons suffering from chronic alcoholism or those who had been drinking before or during exposure to carbon tetrachloride.

Carbon tetrachloride is potentially toxic on inhalation, on contact with the skin or mucous membrane, or orally. Toxicity may result from a single brief exposure to a highly concentrated vapor or prolonged, excessive, or repeated exposure. Immediate symptoms of carbon tetrachloride poisoning due to inhalation include dizziness, giddiness, headache, and occasional nausea, while those symptoms due to ingestion include nausea, vomiting, and diarrhea. Other, even later signs and symptoms following inhalation or ingestion are abdominal pain, jaundice, hematemesis, progressive oliguria, and pericarditis. Generally, the symptoms and signs of carbon tetrachloride poisoning are similar to the ones appearing in various stages of hepatitis, nephritis, and congestive heart failure. In fatal cases of carbon tetrachloride poisoning, necropsy usually reveals pulmonary edema, which occurs during lower nephron nephrosis. A small percentage of victims die from liver disease or subacute yellow atrophy, while some die as the result of toxic potassium blood levels.

Because they presume numerous cases of carbon tetrachloride poisoning are unrecognized, Myatt and Salmons propose that, in every case of jaundice, nephritis, or congestive heart failure in which the patient has no previous history of involvement or in which no apparent cause is found, the patient be quizzed by his examining physician regarding the use of solvents and cleaning solutions. Moreover, as a matter of precaution, it is believed that certain patients should neither use nor be exposed to carbon tetrachloride, namely those who are alcoholic, obese, or undernourished, those with pulmonary disease, cardiac disease, hypertension, peptic ulcer, hepatitic or renal disease, and persons definitely known to be hypersensitive to carbon tetrachloride and other chlorinated hydrocarbons.

## THE CANCER PROBLEM

In his presidential address before the American Association for Cancer Research, Steiner [1] quoted some statistics relative to cancer morbidity and mortality in the United States. It appears that the present cancer mortality is over 200,000 per year and that it is increasing at the rate of approximately 3%, or about 5,000 per year, owing to the fact that a greater number of persons live into the older age groups. In 1948, a total of 207,721 deaths were reported from cancer and leukemia. These figures do not represent the mortality and the total number of cases of cancer, as these are merely cases reported on death certificates. It is pointed out that in the vital statistics cancer may be both over-reported and under-reported. The over-reporting is due to false diagnosis of cancer and probably does not amount to more than 5% of the reported cases. Under-reporting may be due (*a*) to deliberate omission on death certificates of cancers that had been correctly diagnosed; (*b*) to failure to report recognized cancers in persons when some other major disease such as pneumonia or heart disease is also present and is reported as the cause of death; (*c*) to failure to diagnose correctly some cancers that have produced symptoms; (*d*) to failure of diagnosis of clinically silent cancers; and (*e*) to failure to report cured cancers. Under-reporting in the vital statistics is much greater than over-reporting, especially in cases of internal types of tumor that are difficult to diagnose. In view of these facts, Steiner believes that the figure of 207,721 cancer mortality reported for the nation is a great understatement of the national cancer mortality and morbidity.

On the basis of his personal necropsy experience and from reports in the literature, Steiner estimates that the failures in diagnosis and correct reporting together equal 20% of the total reported, or about 41,500 cases for 1948. According to this method of calculation, the total mortality was nearly 250,000 in 1948. When to this figure are added the estimated total patients cured during the year, or 23,000, plus the number of silent or subclinical cancers present in all persons who died during 1948, which amounts to 14,500 subclinical, the sum total for 1948 would be 286,721. This figure probably represents underestimation rather than overestimation. The figure for cancer prevalence, that is, the total cases

1. Myatt, A. V., and Salmons, J. A.: Carbon Tetrachloride Poisoning, A. M. A. Arch. Indust. Hyg. **6**: 74 (July) 1952.

1. Steiner, P. E.: An Evaluation of the Cancer Problem, Cancer Research **12**: 455-464 (July) 1952.

present at any time, is much greater than the annual total, because average survival is more than one year.

On the basis of his experience with 8,000 necropsies performed in the department of pathology of the University of Chicago and with 35,293 necropsies performed at the Los Angeles County Hospital, Steiner was able to estimate that 91.3% of all cases were represented by the 20 commonest types of cancer. As to percentages of cure, these ranged from a high of 85% for skin cancer (including basal cell carcinoma but excluding malignant melanoma) down through 20% for cancers of the larynx, uterus, and mammary gland, to a low of less than 1% for cancers of the pancreas, gallbladder, and liver and for the malignant lymphatic diseases.

It is, of course, well known that present actual rates of cure in many cancers lag behind the theoretical, that is, the levels that would prevail if all available knowledge were used. Steiner points out that the difference between the two levels, actual and theoretical, represents a complex problem composed of educational, psychological, economic, and other factors. The consensus seems to be that the most significant of these is the educational factor. The present status can probably be best formulated by stating that, even if all available knowledge on the eradication of neoplasms could be applied, a large mortality would still remain. This represents the research problem confronting both clinicians and laboratory workers. The ultimate conquest of cancer is not only a therapeutic and educational problem but an investigative problem as well. A large educational effort, on the part of both lay and professional persons, by utilizing all presently available knowledge could result in a considerable improvement in control of some types of cancer but not of others. The residual mortality, after full application of all control knowledge now available, represents the magnitude of the research problem.

## CHLOROTETRACYCLINE AND OXYTETRACYCLINE

The fact that aureomycin and terramycin have an essentially similar spectrum of antibiotic activity and that preliminary studies indicated many similarities in chemical and physical properties at one time posed the question as to whether the two were not identical. Independent studies, in which dissimilar methods were used, have now established beyond reasonable doubt that the two compounds have very similar but not identical chemical structures.[1] Both compounds possess a common four-ringed skeleton, for which the generic term tetracycline has been proposed. They differ only in that aureomycin has a chlorine atom at ring one while terramycin has a hydroxyl group at ring three. The chemically descriptive generic names chlorotetracycline and oxytetracycline, respectively, have therefore been proposed for the two compounds.

1. Hochstein, F. A., and others: Terramycin: VIII. The Structure of Terramycin, J. Am. Chem. Soc. **74**: 3708, 1952. Waller, C. W., and others: Degradation of Aureomycin: IV. Aureomycin and Anhydroaureomycin, ibid. **74**: 4981, 1952.

## THERAPEUTIC APPLICATION OF HEAT

Few procedures are more commonly utilized in homes and hospitals than the application of heat. When heat is employed for therapeutic purposes, it is applied by radiation, conduction, or convection from a heated source and by conversion. In conductive heating energy is transferred by direct contact from the warmer to the cooler subject; it includes such homely methods of heating as hot water bottles, electric pads, and blankets as well as the more elaborate whirlpool baths and therapeutic tanks and pools. Radiant heating is derived from luminous and nonluminous infra-red generators. To some extent heating by convection takes place when these sources are used. Luminous generators of infra-red utilize the radiant energy produced by carbon or tungsten filament bulbs, aided by suitable reflecting surfaces.

Diathermy is among the most widely practiced methods of heating by conversion. In this case high frequency electric current is converted into heat owing to the resistance of the tissues to the flow of current; and of the three available forms, short-wave diathermy is the most popular, microwave diathermy the newest, and long-wave diathermy the oldest. In whatever form diathermy is used or however it is applied, it has no specific biological effects and its therapeutic results are due entirely to the production of heat. Protagonists of long-wave diathermy maintain that it localizes heat more effectively than does short-wave diathermy and that it is more useful in the treatment of chronic inflammatory lesions. Nevertheless, short-wave diathermy enjoys considerable favor precisely because it produces with convenience and safety a more rapid, deeper penetration of heat than does long-wave diathermy.

According to Piersol,[1] thermotherapy is most useful when combined with other well-established measures in the therapeutic regimen. The use of radiant heat and hot compresses in the management of muscular and fascial inflammation is almost routine, while in acute poliomyelitis pain is frequently relieved by hot packs. In properly selected cases of chronic arthritis, baking, hot compresses, whirlpool baths, general hot baths, and paraffin baths administered locally have proved beneficial; however, diathermy has been less frequently employed in giving relief to the arthritic patient.

As in the case of all effective forms of therapy, it is best to exercise caution in the use of thermotherapy. The more intense forms of heating should be administered discreetly in the instance of very young children, old persons, in patients who are debilitated, and in those afflicted with such chronic disorders as diabetes, general arteriosclerosis, myocardial degeneration, and chronic nephritis. Heat should not be applied locally to areas of malignant degeneration nor administered to patients afflicted with hemorrhagic disorders. In general, patients should be advised against administering diathermy in their own homes and on their own responsibility.

Finally, diathermy is contraindicated in acute inflammatory or suppurative processes associated with fever, during profuse menstruation, and in the presence of cancer. Heat may increase pain and disability when applied during the acute stages of trauma, sprains, fractures, and in acute bursitis and arthritis. Disastrous re-

1. Piersol, G. M.: Therapeutic Application of Heat: Its Uses and Abuses, New England J. Med. **247**: 346 (Sept. 4) 1952.

sults have ensued when heat was applied locally to the extremities of patients with impaired peripheral circulation. Disregard of some of the basic physiological changes that occur in the body when heat is used is often responsible for indifferent clinical results and for unwarranted criticism of thermotherapy.

In many conditions the use of heat alone cannot be considered as adequate therapy and other procedures such as massage and, especially, therapeutic exercise should be instituted. For example, heat may assist in bringing about relief of pain in humeroscapular periarthritis, but, if limitation of motion is present, proper exercise must be prescribed to help the patient gain painless full range of motion. Poliomyelitis patients usually receive hot packs or heat from some other source. Patients with this disease showing muscular and fascial tightness and paralysis should receive medically prescribed therapeutic exercises designed to stretch out tightened structures, to provide so-called muscular reeducation, and to strengthen the weakened muscles. The use of heat alone in chronic low back pain due to nonspecific myofascitis may help in the relief of this pain, but, again, possibly massage and certainly properly prescribed therapeutic exercises should be instituted to strengthen the back musculature that has become weak from disuse. If this is not done, the further use of these weakened muscles can lead only to repeated strain and the recurrence of pain.

## CHEMOTHERAPY AND INTRACELLULAR TUBERCLE BACILLI

Dennis and his co-workers [1] produced generalized tuberculosis in Syrian hamsters (Cricetus auratus) by inoculating them subcutaneously with 0.01 mg. of virulent H37Rv tubercle bacilli. The characteristic lesion of tuberculosis in the hamster appeared to be a hard tubercle composed of epithelioid cells containing numerous bacilli. Microscopic studies showed all lesions to consist of compact epithelioid nodules with abundant intracellular acid-fast bacilli. Intra-alveolar nodules of large mononuclear cells with intracellular bacilli were noted in the lungs. Giant cell formation, necrosis, and caseation were minimal.

The type of the disease produced in the golden hamster, the authors state, offers the optimum condition for testing the efficacy of chemotherapeutic agents against intracellular tubercle bacilli in the progressing epithelioid cell tubercle without interference by hypersensitivity, excessive caseation, or inflammatory reactions, with their concomitant local disturbances of tissue and cellular permeability, pH, blood, and lymph supply.

Tuberculous golden hamsters treated with streptomycin or with sodium salt of *p*-aminosalicylic acid showed a therapeutic response in the form of increased survival time and retardation of the tuberculous process, but death from proliferative pneumonia was not prevented.

This particular aspect of chemotherapy of tuberculosis is not new. Wells and Long, as quoted by Sir Howard Florey, stated that if one wishes to destroy the tubercle bacilli in the body by specific chemotherapeutic measures, he must consider not only what chemicals can kill the bacilli in the test tube but also which ones can penetrate the tubercle and pass through the wall of phagocytes in which the bacilli are so often entrenched. Florey [2] believes that penetration of a drug into phagocytic cells before or after they had acquired a population of tubercle bacilli is accomplished in three ways: by the phagocytosis of the particles, by the selective uptake of large molecules analogous with the vital dyes, or by a less specific passage of substances through the cell membrane.

Mackaness has devised a method making it possible to observe in vitro for many days the effect on tubercle bacilli that are contained within rabbit macrophages of drugs dissolved or suspended in the surrounding fluid medium. Macrophages were obtained from the peritoneal cavity of rabbits following the instillation of liquid paraffin, and these were parasitized with the virulent bovine Branch strains or with the human strain H37Rv of Mycobacterium tuberculosis grown in liquid tween®-albumin medium. Infection was effected by centrifuging a suspension of macrophages in fresh rabbit serum to which had been added a highly dispersed suspension of tubercle bacilli in Dubos-Davis medium. Seventy per cent of the macrophages obtained in this way were infected. The intracellular bacilli within the isolated mammalian macrophages, kept at 37 C, were seen to multiply after about 48 hours of incubation. The onset of growth is followed soon by death and lysis of the macrophage host cell. Uninfected macrophages will remain alive and in apparently normal condition for long periods. The proliferation of intracellular tubercle bacilli and the lysis of the host cell that attends it can be wholly reversed by a sufficient concentration of streptomycin. Thus it is possible to demonstrate that streptomycin can pass into the macrophage and stop the intracellular growth of virulent microbacteria. However, the concentration of streptomycin that had to be present in the fluid around the macrophages in vitro in order to inhibit the growth of intracellular organisms is considerably greater than that required to inhibit the growth of tubercle bacilli in the Dubos-Davis medium. The growth is fully inhibited only by a concentration considered to be above that which can be maintained for any length of time in body fluids.

Of the various antituberculous drugs tested in this manner, most showed a pronounced reduction in activity against intracellular bacilli. Mackaness and Smith [3] demonstrated that of the drugs tested isoniazid (isonicotinic acid hydrazide) is equally active against intracellular bacilli and those grown in Dubos-Davis medium.

This method of examining antituberculous drugs, Florey thinks, may be of considerable value in estimating their possible performance in vivo, as it separates out one factor for study, namely, the behavior of the drugs toward intracellular bacilli.

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1. Dennis, E. W.; Goble, F. C.; Berberian, D. A., and Frelih, E. J.: Experimental Tuberculosis of the Syrian Hamster (Cricetus Auratus), Ann. New York Acad. Sc. **52**: 646-661 (Dec. 14) 1949.

2. Florey, H.: Walter Ernest Dixon Memorial Lecture: Some Problems in the Chemotherapy of Tuberculosis, Proc. Roy. Soc. Med. **45**: 71-78 (Feb.) 1952.

3. Mackaness, G. B., and Smith, N.: The Action of Isoniazid (Isonicotinic Acid Hydrazide) on Intracellular Tubercle Bacilli, Am. Rev. Tuberc. **66**: 125-133 (Aug.) 1952.

# ORGANIZATION SECTION

## THE NEW YORK SESSION

Arrangements for the various activities at the New York Session, June 1-5, 1953, are progressing rapidly. General headquarters and registration for the meeting will be at Grand Central Palace.

### THE SCIENTIFIC EXHIBIT

Applications for space in the Scientific Exhibit at the New York Session will close on Jan. 9, 1953. Prospective applicants are requested to submit their applications as far in advance of that date as possible, however. All applications received after the closing date will be placed on the waiting list, to be considered if space becomes available.

The Scientific Exhibit will be located on the fourth floor of Grand Central Palace. Exhibits will be arranged, as far as possible, in groups corresponding to the Sections of the Scientific Assembly. Application blanks may be obtained from the Section representatives or from the Director, Scientific Exhibit, American Medical Association, 535 N. Dearborn St., Chicago 10, Ill.

### SECTION MEETINGS

Meetings of the 20 Sections of the Scientific Assembly will be held in the ballrooms of hotels adjacent to Grand Central Palace. The program for each Section is in charge of the Section secretary.

### COLORED TELEVISION

Colored television will originate in one of the hospitals in the vicinity of the Grand Central area and will be shown in a hotel ballroom where proper facilities can be obtained. Smith, Kline and French will again sponsor the program under the guidance of the Committee on Colored Television.

### MOTION PICTURES

An outstanding program of motion pictures will be shown in the ballroom of one of the hotels near Grand Central Palace. No application blanks for time on the motion picture program have been distributed, but physicians interested in submitting films should communicate directly with the Secretary, Committee on Medical Motion Pictures, American Medical Association, 535 N. Dearborn St., Chicago 10, Ill.

## CONVERSION OF DIATHERMY APPARATUS

Physicians and hospital administrators have requested information on converting diathermy apparatus to meet the rules and regulations of the Federal Communications Commission with respect to frequency control and radio interference; hence, from time to time information bearing on the 1947 Ruling of the FCC has been made available to the medical profession through THE JOURNAL.

Recently, an item appeared in the Washington News section of THE JOURNAL reporting that the Defense Department had announced a saving of approximately $148,500 by the modification of diathermy equipment used by Army and Air Force medical units. The estimated cost of new equipment would have been $184,000. It was reported that 450 noncomplying diathermy apparatus were modified for $80.00 per unit, or a total cost of only $36,000.

This cost was at variance with other estimates that had come to the attention of the Council on Physical Medicine and Rehabilitation, and it seemed advisable to make additional inquiries. Experts had advised the Council that it would be less expensive for physicians to acquire new diathermy appliances already tested, FCC tested, and complying with the rules and regulations of the FCC than to modify a noncomplying unit. This was regarded as an unreasonably expensive procedure, which might be unsatisfactory, especially if each unit were modified separately.

On inquiry, it was ascertained that 450 diathermy appliances of the same make and model had been converted in hospitals in which they were being used. These appliances were crystal-controlled and when purchased by the armed forces met the FCC rules existing then. Furthermore, these had been manufactured for the armed services during World War II, in accordance with federal specifications that existed at that time. These specifications incorporated the frequency control requirements for diathermy equipment adopted in 1947 in the rules and regulations of the FCC; therefore, the problem of conversion was to provide sufficient shielding to comply with the FCC requirements of harmonic suppression. Since these units were already built to meet most of the revised requirements, the one change necessary was the replacement of the crystal. The office of the Defense Department obtained type approval from the FCC for conversion engineering and design.

As previously reported, the Council has been informed by reliable agencies that the conversion of short wave diathermy equipment not originally designed with frequency control is a difficult electrical and mechanical procedure. The costs involved are as much, if not more, than the cost of replacing the equipment with Council-accepted and FCC type approved apparatus.

Units built prior to the 1947 FCC rules and regulations were not designed with the proper shielding or frequency control to allow them to be easily or reasonably converted to meet present requirements. The armed forces' inexpensive adjustment of frequency was possible only because of the slight revision of the rules and regulations.

Physicians desiring additional information on the conversion of diathermy equipment might well consult the Engineering Department of the FCC in Washington, D. C.

## PRINTS AVAILABLE OF "YOUR DOCTOR" FILM

Sixteen millimeter prints of the movie-short film entitled "Your Doctor" will be available for showing to schools, clubs, civic groups, industrial plants and special professional meetings after Jan 1. Produced by Louis de Rochemont in cooperation with the A. M. A., this film portrays the work of 35-year-old Dr. George Bond in his valley clinic in rural North Carolina. The American Medical Association also has made arrangements to obtain prints for state and county society film libraries. Societies interested in purchasing a print at cost may write to the A. M. A. Public Relations Department. An estimated 12 million persons viewed this film in theaters across the nation in 1952.

## NEW AMA PUBLICATION

The Committee on Medical Motion Pictures announces the publication of a revised film list that includes 78 medical films that are not readily available from other sources. This list is now available, and copies may be obtained by writing to the Committee on Medical Motion Pictures, 535 N. Dearborn St., Chicago 10, Ill.

## COMMITTEE ON BLOOD

The secretariat of the Committee on Blood has been moved to the Headquarters Office from the Washington Office. Dr. Paul L. Wermer has been appointed Secretary of the Committee, and all communications should be addressed to him at the American Medical Association's headquarters, 535 N. Dearborn St., Chicago 10, Ill.

# MEDICAL NEWS

## ARKANSAS

**Award to Dr. Day.**—Paul L. Day, Ph.D., head of the biochemistry department, University of Arkansas School of Medicine, Little Rock, has won the 1952 Southwest award of the American Chemical Society, consisting of a bronze plaque and $200 in cash. Dr. Day, who is an affiliate member of the American Medical Association, has served as chairman of the School of Medicine's research committee, the committee on postgraduate education, and the fellowship board. He is the author of many scientific papers, chiefly in the field of vitamins and nutrition; was associate editor of the *Journal of Nutrition*, 1948-1952; and at present is associate editor of the *Proceedings of the Society for Experimental Biology and Medicine*.

## CALIFORNIA

**Fund for Memorial Library.**—A fund is being raised to establish a medical library at the Hemet Community Hospital as a memorial to the late Dr. Leslie J. Clark, a past president of the Riverside County Medical Society, who was president of the board of the hospital and chairman of its medical staff at the time of his death. The hospital is donating space and furnishing shelves and cases for the library, which will be available to members of the medical staff. Contributions may be sent to Mrs. Grace Scott, committee secretary.

**Cardiorespiratory Laboratory.**—A $150,000 cardiorespiratory laboratory has been established in the Hospital of the Good Samaritan by the University of Southern California School of Medicine, Los Angeles. The laboratory, made possible by gifts from businessmen and physicians, will do research into the causes and treatment of asthma, cancer and tuberculosis of the lungs, silicosis, and emphysema, and the effect of smog on the human respiratory system. Private, industrial, and charity patients will be accepted from all physicians. One of the laboratory's major functions will be the instruction of local physicians in the most efficient methods of diagnosis and treatment of pulmonary diseases.

**Personal.**—At the annual meeting of the Los Angeles County Branch of the American Cancer Society, Dr. Ian G. Macdonald, assistant clinical professor of surgery, University of Southern California, Los Angeles, received the American Cancer Society's distinguished service medal for his services in the field of cancer control. Dr. Macdonald is chairman of the Cancer Commission of the California Medical Association.——Dr. Myron Prinzmetal, director of research at the Cedars of Lebanon Hospital, Los Angeles, has been appointed to the advisory council to the National Heart Institute of the U. S. Public Health Service, Washington, D. C.——Wendell M. Stanley, Ph.D., director of the Virus Laboratory, University of California at Berkeley, has been appointed to the National Advisory Cancer Council of the U. S. Public Health Service. Dr. Stanley in 1946 was awarded a Nobel prize in chemistry for isolating the virus of the tobacco mosaic disease in crystal form. He received a presidential certificate of merit in 1948 for the development of the centrifuge type of influenza vaccine.——Dr. Irving D. Litwack, city health officer at Long Beach, has been awarded a certificate of merit by the Prudential Insurance Company for pioneer child safety work, specifically in the region of home accidents.

## CONNECTICUT

**Rare Obstetric Books.**—Dr. Alfred M. Hellman, New York, has loaned to the Yale Medical Library, New Haven, his collection of 38 editions of the famous 16th century "Rosengarten" obstetric books. Written in the vernacular instead of in Latin, this book by the German physician Eucharius Roesslin had enormous influence on the practices of midwives and surgeons of that time. Roesslin's great contribution to medicine was his fight against ignorance and superstition concerning childbirth.

## IDAHO

**State Medical Election.**—At the annual meeting of the Idaho State Medical Association in Sun Valley, Dr. Wallace Bond, Twin Falls, was installed as president; Dr. Eugene V. Simison, Pocatello, was elected president-elect; and Dr. Robert S. McKean, Boise, was reelected as secretary-treasurer.

## ILLINOIS

**Dr. Cross Reappointed Director of Public Health.**—Governor-elect William G. Stratton has announced that Dr. Roland R. Cross, Springfield, will remain as state director of public health. Dr. Cross, who joined the health department in 1933, has been a cabinet officer under four governors. After being appointed director in 1940 by Gov. Stelle, he was retained by Gov. Green and by Gov. Stevenson. The new appointment is for two years.

### Chicago

**Grant for Poliomyelitis Research.**—The University of Chicago has received a March of Dimes grant of $35,575 from the National Foundation for Infantile Paralysis. This is the sixth grant in as many years for research at the University of Chicago into the chemical and life processes of viruses.

**Personal.**—Dr. Derrick T. Vail, professor of ophthalmology, Northwestern University Medical School, has been appointed to the National Advisory Neurological Diseases and Blindness Council, according to an announcement by the Surgeon General, U. S. Public Health Service.——Dr. Frederick R. Schmidt, associate professor of dermatology, Northwestern University Medical School, has been granted a leave of absence for the year 1952-1953 to study in Central America.——Dr. Mark T. Goldstine has celebrated his 50th anniversary as a member of the medical staff at Wesley Memorial Hospital. Dr. Goldstine, chairman emeritus of Wesley's department of obstetrics and gynecology, serves as a member of the hospital board of trustees.——Dr. Frederick J. Lesemann Sr. was guest of honor at a testimonial dinner given by the medical staff and board of trustees of Englewood Hospital. Dr. Lesemann, who is retiring after 42 years of service, was presented with a gold watch bearing the following inscription: "Presented to Dr. Frederick Lesemann Sr., in recognition of his many years of loyal, faithful and diligent service in Englewood Hospital." Dr. and Mrs. Lesemann plan to live in California.

## INDIANA

**State Medical Election.**—At its annual convention in Indianapolis the Indiana State Medical Association installed Dr. Paul D. Crimm of Evansville as president and chose Dr. William H. Howard, Hammond, president-elect, Dr. Roy V. Myers, Indianapolis, treasurer, and Dr. James W. Denny, Indianapolis, assistant treasurer.

**Dr. Johnson Day.**—In honor of Dr. Jess J. Johnson, the citizens of Milltown and community inaugurated Dr. Johnson Day with a parade led by the Corydon High School Band. Dr. Johnson was given a clock with the inscription of the day and a motorized truck for use on his farm. A portrait of Dr. Johnson was presented to his wife.

**Personal.**—In recognition of his outstanding service to the community, Dr. William A. Miller has been elected to honorary membership in the Hagerstown Rotary Club.——Dr. Oran A. Province, Franklin, was recently awarded a certificate of distinction and a 50 year pin by the Indiana State Medical Association.——Dr. Herbert S. Gaskill, professor of psychiatry, Indiana University School of Medicine, Indianapolis, has been named director of psychiatric services and professor of psychi-

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

atry at the University of Colorado School of Medicine, Denver, to succeed Dr. Franklin G. Ebaugh, who retired Jan. 1. Dr. Gaskill previously served on the faculties of Jefferson Medical College of Philadelphia and the University of Pennsylvania School of Medicine, Philadelphia, and as psychiatrist at the Hospital of the University of Pennsylvania. During World War II, he was chief of the neuropsychiatric section of the 20th General Hospital that originated from the University of Pennsylvania and was a neuropsychiatric consultant to the Surgeon General.

## MAINE

**President of Jackson Laboratory.**—Dr. Frank E. Adair, attending surgeon emeritus of the Memorial Center for Cancer and Allied Diseases, New York, and a past president of the American Cancer Society, has been named president and board chairman of the Roscoe B. Jackson Memorial Laboratory at Bar Harbor.

**Outbreak of Streptococcic Sore Throat.**—Dr. Dean H. Fisher, of the Maine Department of Health and Welfare, has reported to the U. S. Public Health Service that some 81 persons became ill from one to three and one-half days after eating oyster stew. Cultures from all cases showed Streptococcus viridans. Cultures from a cook who had a purulent discharge from a cut thumb showed the same type of organism.

## MICHIGAN

**Personal.**—Dr. Edward F. Ducey, pathologist at St. Mary's Hospital, Grand Rapids, has resigned to accept a similar post in Ventura, Calif.——Dr. Frank H. Bethell, assistant director, Thomas Henry Simpson Memorial Institute for Medical Research, University of Michigan, has been named chairman of the U. S. P. Anti-Anemia Preparations Advisory Board.

**Classes for Expectant Mothers.**—The Dearborn Medical Society announces the following schedule of six week prenatal classes for expectant mothers: West Dearborn, classes held at YWCA (Monroe, south of Michigan) start Jan. 13, March 23, and May 4. East Dearborn, classes held at Health Department (Carmen Theatre Bldg., Schaefer Rd., north of Ford Rd.) start Jan. 14, March 24, and May 5. Detroit physicians may refer patients who live in Dearborn and its surrounding areas. Patients wishing to enroll should call LUzon 1-1200.

## MISSISSIPPI

**Society Election.**—At the annual meeting of the Mississippi Pediatric Society Dr. Charles R. Gillespie, Laurel, was elected president, and Dr. Jim G. Hendrick, Jackson, secretary. The next annual meeting will be held in Biloxi May 13.

## MISSOURI

**University News.**—Dr. Philip H. Starr, instructor in psychiatry, Washington University School of Medicine, St. Louis, has been appointed acting director of the Washington University Community Child Guidance Clinic. Dr. Starr will continue as chief psychiatric consultant to the St. Louis Children's Hospital and director of the Children's Mental Health Clinic. Dr. Donald Meltzer, former director of the Child Guidance Clinic, is on temporary leave in the U. S. Army Air Force.

**Appointments in Department of Medicine.**—Dr. Philip A. Tumulty, associate professor of medicine, Johns Hopkins University School of Medicine, Baltimore, has been appointed director of the department of internal medicine at St. Louis University, effective next spring. Dr. Tumulty's appointment marks the first time a full-time head of the department of internal medicine has served at the university. Dr. Charles G. Zubrod, formerly assistant professor of medicine and assistant professor of pharmacology and experimental therapeutics at Johns Hopkins School of Medicine, will be associate professor of internal medicine to assist research development in the department, and Dr. Thomas E. Van Metre Jr., postdoctorate fellow in medicine and assistant physician at Johns Hopkins School of Medicine, will be assistant professor of internal medicine.

## MONTANA

**State Medical Election.**—At its annual meeting in Missoula, the Montana Medical Association installed Dr. James M. Flinn, Helena, as president and chose Drs. D. Ernest Hodges, Billings, president-elect; Sidney C. Pratt, Miles City, vice-president; and Everett H. Lindstrom, Helena, secretary-treasurer.

**Society News.**—At the annual meeting of the Montana Public Health Association in Sidney, Dr. Walter G. Tanglin of Polson was elected president and Lt. Burton K. Kilbourne, Helena, was reelected secretary.——At a recent meeting of the Yellowstone Valley Medical Society, Dr. Roger A. Larson, Billings, was elected president; Dr. Richard E. Brogan, Billings, vice-president; and Dr. John T. Hurly, Billings, secretary. Dr. John J. Hammerel, Billings, was reelected treasurer.——The Montana Radiological Society was recently formed, with Dr. Walter B. Cox, Missoula, as president and Dr. Grant P. Raitt, Billings, as secretary-treasurer.

## NEVADA

**State Medical Election.**—At its recent annual meeting in Reno the Nevada State Medical Association installed Dr. Leslie A. Moren of Elko as president and chose Drs. Dwight L. Hood and Frederick M. Anderson, Reno, first and second vice-presidents, respectively, Dr. William A. O'Brien III, Reno, secretary-treasurer, and Drs. Edwin L. Cantlon, Reno, J. Vernon Cantlon, and George A. Collett of Elko, members of the board.

## NEW YORK

**Hospital News.**—Dr. John M. Benny, Buffalo, assistant director of clinics of the Edward J. Meyer Memorial Hospital since January, 1951, has been named assistant superintendent of the hospital to succeed Dr. Sarkis J. Anthony, who has become superintendent.

**Lecture on Adrenal Cortical Function.**—The Medical Society of the State of New York with the cooperation of the New York State Department of Health will present a lecture on "Clinical Applications of Newer Physiological Concepts of Adrenal Cortical Function" by Dr. Charles W. Lloyd, assistant professor of medicine, State University of New York College of Medicine at Syracuse, at the Hotel Utica in Utica Jan. 15 at 8:30 p. m.

**In Memory of Dr. Hazard.**—The staff of the Veterans Administration Hospital, Albany, paid honor to the late Dr. John D. Hazard, senior resident in surgery at the hospital, by unveiling a plaque in his memory and presenting a savings bond to his son, John, 7. A veteran of World War II, Dr. Hazard at the time of his death was completing graduate training in surgery at the hospital and was scheduled to become a full-time staff general surgeon there.

**Review of Laws Governing Mental Patients.**—Governor Dewey has requested the New York State Mental Hygiene Council to undertake a thorough review of New York laws and procedures governing the release of mental patients. The study will embrace three phases: (1) a statistical analysis of case records to determine the current proportion of crime among released mental patients as compared with crime in the general population; (2) an evaluation of present procedures, to be based on actual professional observation in the hospitals; and (3) a comprehensive study of the laws and rules governing the release of the patients.

**Grants to Alcoholic Clinics.**—A grant of $9,000 for the development of community services for chronic alcoholics has been awarded by the New York State Mental Health Commission to the University of Buffalo Information and Rehabilitation Center for Alcoholism, and a grant of $11,778 has been given to a new clinic, which, under professional direction of the State University of New York College of Medicine at Syracuse, will be operated by the Syracuse Dispensary, Inc. Policies of this new clinic will be determined by a joint committee. Plans for staffing the clinic call for an internist, a psychiatrist, a clinical psychologist, a psychiatric social worker, a public health nurse, a stenographer, and a part-time clerk. The Mental Health Com-

mission staff is currently considering proposals for the development of additional clinic services in Rochester and New York City.

**Society News.**—At a recent meeting the Brooklyn Dermatological Society elected Dr. Samuel I. Greenberg, president; Dr. Camillo B. Locasto, vice-president; and Dr. Harry L. Feigenbaum, secretary.——At its recent meeting the Long Island Psychiatric Society was addressed by Dr. Nathan S. Kline, director of research at Rockland State Hospital, Orangeburg, who discussed "The Interdisciplinary Approach to the Study of Personality Organization."——The New York Allergy Society has elected Dr. Paul F. DeGara, New York, president; Dr. Frederick R. Brown, New York, president-elect; Dr. William B. Sherman, New York, vice-president; Dr. Murray M. Albert, Brooklyn, secretary; and Dr. Samuel J. Prigal, New York, treasurer.

**Presbyterian Hospital Unit Dedicated.**—The Strong Memorial Wing for Children, adjoining the Mary Harkness Convalescent Home in Port Chester, has been dedicated. It will accommodate 22 handicapped children whose families are not able to provide convalescent care following poliomyelitis, orthopedic and medical conditions, and surgical procedures. The wing, given in memory of Martha Moulton Strong, who died in 1918 at the age of 9, was made possible under the terms of the will of her father, the late William E. S. Strong, consulting engineer and former corporation member of the Presbyterian Hospital. Built at a cost of $250,000, it completes the convalescent service at the Port Chester unit, which is under the direction of the attending staffs of the Presbyterian Hospital. Dr. Herbert F. Wilshusen of Port Chester is the attending physician for the Mary Harkness Convalescent Home and Strong Memorial Wing.

### New York City

**Hospital News.**—On Jan. 9 at 3 p. m. the Division of Neoplastic Diseases, Montefiore Hospital, will present a lecture on "The Developmental Concepts of Uterine Cancer" by Dr. Saul B. Gusberg, assistant professor of gynecology and obstetrics, Columbia University College of Physicians and Surgeons.

**Tumor Conference.**—Harlem Hospital will present its monthly tumor clinic conference lecture Jan. 22 at 8:30 p. m. in the Women's Pavilion (137th St. entrance). Dr. Howard C. Taylor Jr., director, obstetric and gynecologic service, Presbyterion Hospital, will speak on "Special Problems in Treatment of Uterine Fibroids."

**Council to Coordinate Health Programs.**—Mayor Impellitteri has announced the creation of an Interdepartmental Health Council to coordinate jurisdictions, policies, and programs of the health, hospitals, and welfare departments in the city health services. Dr. Marcus D. Kogel, commissioner of hospitals, has been appointed chairman of the council through Dec. 31, 1953, and Dr. John F. Mahoney, commissioner of health, and Mr. Henry L. McCarthy, commissioner of welfare, have been designated associate members. In letters to the three commissioners, the mayor stated that "besides the existing problems of overlapping jurisdictions and policy which may be solved through the efforts of the council, studies and recommendations concerning all health needs of the city should be made."

**Dr. Rusk Receives Criss Award.**—The Mutual Benefit Health and Accident Association of Omaha has named Dr. Howard A. Rusk, director of the Institute of Physical Medicine and Rehabilitation of the New York University-Bellevue Medical Center, as the 1952 winner of its $10,000 Dr. C. C. Criss award and gold medal in recognition of his work in rehabilitating the physically handicapped. In announcing the award, Mr. V. J. Stutt, president of Mutual of Omaha, said: "Dr. Rusk has helped bring new hope to a hitherto helpless and defeated segment of our population, the some 23 million physically handicapped. Probably more than any other American, he has demonstrated that the physically handicapped can be taught to become socially and economically self-sufficient. The production capacity added to our economy through his work alone would be a tremendous figure. The worth of salvaging human lives through his endeavors cannot be measured."

**Cornerstone Laid for Experimental Institute.**—The cornerstone for the Henry W. and Albert A. Berg Institute for Experimental Physiology, Surgery and Pathology at the New York University-Bellevue Medical Center was laid Dec. 3. A check for $500,000 for construction of the institute was presented to Mr. Winthrop Rockefeller, chairman of the Medical Center Board of Trustees, by a representative of the estate of the late surgeon Dr. Albert A. Berg. The will also provides a fund of over a million dollars for maintenance of the institute, named for him and his elder brother, Dr. Henry W. Berg, who died Dec. 21, 1938. At a meeting of the joint faculties of the New York University College of Medicine and the New York University Post-Graduate Medical School following the cornerstone-laying, Dr. John H. Mulholland, chairman of the department of surgery of the college of medicine, spoke on the plans and programs of the Berg Institute, stating that, in creating the institute, Dr. Berg "contemplated a workshop where physiology and pathology would contribute nutriment for the growth of surgery." The six story institute building adjoins the center's new medical science building, for which the cornerstone was recently laid. The two new buildings are scheduled for completion next fall. The first completed unit in the Medical Center's 25 million dollar building program, a four story structure facing 34th St., houses the center's Institute of Physical Medicine and Rehabilitation.

**Betatron for Treatment of Cancer.**—The Physiology Laboratory-Betatron Building, recently dedicated as a unit of the Memorial Center for Cancer and Allied Diseases, is located at 410 E. 68th St. In the four story structure are a 24 million electron volt betatron and extensive laboratory facilities. The betatron, the first to be designed specifically for treatment of cancer, is said to be about 12 times more powerful than the most powerful conventional x-ray machines. The annex in which it is installed has walls of concrete weighing 3,500 lb. to the cubic yard. The machine is 14 ft. high, weighs 5 tons, and is approached by way of a concrete maze around which the rays cannot travel. The floor of the physiology building that connects with the betatron annex will be used for studies related to the betatron and other investigations concerning the radiation treatment of cancer. It contains five laboratories, a calculating room, a storage and work room, a special dark room for developing films used as measurement devices for the betatron, an air-conditioned animal-care room for irradiated animals, and an examining room for patients. This new 1½ million dollar laboratory-betatron unit was made possible by a grant-in-aid for cancer research construction, awarded through the National Cancer Institute by the U. S. Public Health Service, and gifts of the Andre and Bella Meyer Foundation and the Samuel H. Kress Foundation. The building completes the construction program begun in 1939, which has added to the center the Strang Cancer Prevention Clinic (1947), Sloan-Kettering Institute (1948), McCann Children's Pavilion and James Ewing Hospital of the City of New York (1950), and the Tower Outpatient Building (1951).

## NORTH DAKOTA

**Society News.**—The North Dakota Diabetes Association, which met in Fargo, elected Dr. Alan K. Johnson, Williston, president; Dr. Robert W. Rodgers, Dickinson, vice-president; Dr. Martin Hochhauser, Garrison, secretary; and Dr. Edgar A. Haunz, Grand Forks, executive secretary-treasurer.

## OHIO

**Health Program on Television.**—The Cleveland Health Museum, in cooperation with the Academy of Medicine of Cleveland, will present a weekly half-hour television show "Prescription for Living," beginning Jan. 4 (4 p. m.) on an all-Ohio hook-up. The half-hour program, sponsored as a public service by the Standard Oil Company of Ohio, deals with a family "typical in that most of its ideas of health and medicine have been gleaned from magazine and newspaper reading, patent medicine claims, old wives' tales, and hearsay." Warren A. Guthrie, Ph.D., Western Reserve University, Cleveland, will interview a guest physician who straightens out the false beliefs in a presentation made visual by exhibits from the workshops of the Health Museum. The academy will invite local physicians and physicians from other

Ohio cities to appear on the programs. "Prescription for Living," originating on station WXEL in Cleveland, will also be carried on stations WTVM, Columbus; WHIO, Dayton; WSPD, Toledo; and WCPO, Cincinnati. Summary sheets of each show will be mailed from the museum on request. The first telecast will cover "The Common Cold."

**Personal.**—The Lakewood Clinical Club, Cleveland, has presented Dr. Walter R. Katzenmeyer with a purse of $1,370. Dr. Katzenmeyer recently reopened his offices in Bay Village after a year-long illness with poliomyelitis.——Dr. Charles A. De Wert, an assistant professor at the Institute of Industrial Health, University of Cincinnati College of Medicine and for 12 years associate medical director of Dunham Hospital, Cincinnati, has been appointed industrial physician for the William S. Merrell Company, Cincinnati.——Dr. Robert Kurzbauer, who is on the staffs of Mount Sinai Hospital, Cleveland, and Marymount Hospital, Garfield Heights, has been appointed associate physician at Montefiore Home.——Dr. Paul Q. Peterson, chief of the Bureau of Local Services of the Ohio Department of Health, has been granted a two year leave of absence to accept a commission as director of the United States Medical Mission to the Chinese Government in Formosa.

**Hospital News.**—The Jewish Hospital Association recently announced the opening of a new department of psychiatry in the hospital and the appointment of Dr. Milton Rosenbaum, professor of psychiatry at the University of Cincinnati College of Medicine, as director of the new facility. The hospital has appointed as director of ophthalmology, Dr. Ira A. Abrahamson, associate clinical professor of ophthalmology at the University of Cincinnati College of Medicine. Dr. Lee S. Rosenberg, who has been assistant director of the radiology department since 1950, has been made full-time director of that department.

**Grant for Study of Bejel.**—Dr. E. Herndon Hudson, Athens, director, Ohio University Health Center, has been awarded a grant by the U. S. Public Health Service to prepare an illustrated monograph on bejel, a form of endemic nonvenereal syphilis found among the Arabs in the Middle East, and first described by Dr. Hudson in 1924. Dr. Hudson will assemble and analyze the material accumulated during 12 years in Deir-e-Zor, Syria, and combine it with information secured while he was serving under the World Health Organization as director of a bejel-syphilis project in Iraq in 1950-1951. During this period he and his associates treated several thousand patients and inoculated rabbits with the disease, so that the germs could be transported to laboratories in this country. The grant is to be used in part for punchcard analysis, nontechnical assistance, travel, and in part for medical assistance for one year in the health center, to release Dr. Hudson for this research. He will remain in active relation to the health center as director.

## PENNSYLVANIA

**Dr. Gardner Becomes Secretary-Treasurer.**—Dr. Harold B. Gardner, formerly professor of therapeutics in the University of Pittsburgh School of Medicine, has taken up his duties in Harrisburg as secretary-treasurer of the Medical Society of the State of Pennsylvania, succeeding Dr. Walter F. Donaldson, Pittsburgh, (*J. A. M. A.* **150:**1128 [Nov. 15] 1952). Dr. Gardner has practiced medicine in Pittsburgh for 33 years. His son, Dr. Weston D. Gardner, is a member of the faculty of Marquette University School of Medicine, Milwaukee.

**Personal.**—Dr. Leslie R. Angus, who for the past six years has been director of psychiatric services at the Devereaux Schools, Devon, has been appointed resident psychiatrist and director of the Child Research Clinic of the Woods School. Dr. Angus is an instructor in psychiatry at the University of Pennsylvania.——Dr. John N. Camp, formerly of Butler, has been appointed full-time physician and surgeon at Oklahoma State Penitentiary, to succeed Dr. Arthur E. Hale, who resigned last July to enter private practice at Hugo, Okla.

## TEXAS

**Course in Economics and Ethics.**—To prepare students for the transition from medical school to private practice, Southwestern Medical School of the University of Texas, Dallas, will offer a course in "Medical Economics and Ethics" during the final six months of the senior year. This course will emphasize economic problems related to medical practice. From experienced physicians the students will learn about the advantages and disadvantages of individual, or solo, practice as compared with group practice of medicine. Considerable emphasis will be placed on the relationship of the practicing physician to the other physicians in his own community and in distant communities and to the role of the physician in county, state, and national medical societies. The contribution of the societies to the physician will also be stressed.

## UTAH

**Press-Radio Television Dinner.**—The Utah State Medical Association was host Dec. 10 to press, radio, and television representatives at a dinner in Salt Lake City, which demonstrated the cordial working relationship between Utah physicians, newspapers, and radio and television stations. Members of the council and the state committee on press relations, made up of five physicians from various sections of the state, also attended. It was the first meeting sponsored by the new press relations committee headed by Dr. Wallace S. Brooke, Salt Lake City, who presided at the dinner together with Dr. Kenneth B. Castleton, Salt Lake City, president of the state society. John L. Bach, Chicago, director of A. M. A. press relations, was the speaker. Besides drafting a code of cooperation with newspapers, radio, and television, the press committee is instituting a health column in 56 weekly papers. The state society also is starting a new nonscientific news bulletin for its members, Jan. 15. A question-and-answer period followed the dinner. The affair stimulated so much interest that the chairman eventually was forced to terminate it, explaining that "if we don't adjourn this meeting, we'll be here all night."

## VIRGINIA

**Lecture on Cervicobrachial Pain.**—On Jan. 14, Dr. J. Hamilton Allan, professor of orthopedic surgery, University of Virginia School of Medicine, Charlottesville, will address the medical staff conference at Winchester Memorial Hospital on "Cervicobrachial Pain."

**Annual Willis Oration.**—Dr. Paul Dudley White, Boston, recently delivered the first annual A. Murat Willis oration on "Personal Experiences in Cardiology" at the Richmond Academy of Medicine Building. The oration was established in memory of Dr. A. Murat Willis, who was instrumental in establishing several independent hospitals in the state. Dr. White, who came to Richmond on invitation of the Johnston-Willis Ex-House Staff Association, was the honor guest at the group's annual dinner meeting at the Commonwealth Club.

**Society News.**—The Virginia Obstetrical and Gynecological Society recently installed Dr. John R. Kight, Norfolk, as president; named Dr. Chester L. Riley, Winchester, president-elect; and reelected Dr. Chester D. Bradley, Newport News, secretary-treasurer.——At its annual meeting, the Virginia Society for Pathology and Laboratory Medicine elected Dr. Martin L. Dreyfuss, Clifton Forge, president; Dr. Arnold J. Rawson, Norfolk, vice-president; and Dr. William D. Dolan Jr., Arlington, secretary-treasurer.——The Virginia Orthopedic Society has named Dr. Prentice Kinser Jr. of Danville, president; Dr. Bernard D. Packer, Richmond, vice-president; and Dr. Allen M. Ferry, Arlington, (reelected) secretary-treasurer.——The Virginia Urological Society recently elected the following officers: president, Dr. Warren W. Koontz, Lynchburg; vice-president, Dr. Thomas B. Washington, Richmond; and secretary-treasurer (reelected), Dr. William R. Jones Jr., Richmond.

**Pediatric Problems.**—A conference on "Problems of Infants and Young Children in General Practice" will be held at the University of Virginia School of Medicine, Charlottesville, Jan. 16. At 3:45 p. m. there will be a panel discussion of household poisons. Preceding this discussion Dr. Joseph R. Bowman, Johnson City, Tenn., will discuss "Obstruction of Alimentary Tract in Newborn Infants." During the morning session Dr. Bowman will speak on "Acute Abdominal Conditions in Infants and Young Children." A paper on "Respiratory Problems in Newborn Infants" will be presented at 2 p. m. by Dr. Stewart H. Clifford, Boston. Presentations by University of Virginia faculty members will include:

Bronchiectasis in Infants and Young Children, Everett C. Drash.
Neurological Procedures in Infants and Young Children, Walter O. Klingman.
Urologic Problems in Infants and Young Children, Samuel A. Vest.
Recent Advances in Treatment of Tuberculous Meningitis in Young Children, William W. Waddell Jr.
Infant Feeding, McLemore Birdsong.
Common Eye Problems in Infants and Young Children, Edwin W. Burton.

Registration may be made through the office of the dean, University of Virginia School of Medicine, Charlottesville.

## WEST VIRGINIA

**Society News.**—The Potomac Valley Medical Society has elected Dr. Milford F. Townsend, Petersburg, president; Drs. Orlando S. Reynolds, Franklin, Vernon L. Dyer, Petersburg, Robert W. Love, Moorefield, James F. Easton, Romney, and James H. Wolverton Sr., Piedmont, vice-presidents; and Dr. Charles J. Sites, Franklin, treasurer.——The Eastern Panhandle Medical Society recently elected the following Martinsburg physicians as officers: Dr. Dudley J. Shaw, president, and Drs. William R. McCune and George F. Pugh Jr., vice-presidents, and reelected Dr. George O. Martin, secretary-treasurer. Dr. William A. Wallace, Martinsburg, was elected a member of the board of censors.

## GENERAL

**Change in Date of Psychosomatic Meeting.**—The annual meeting of the American Psychosomatic Society, originally scheduled for May, will be held April 18-19 at Chalfonte-Haddon Hall in Atlantic City, N. J.

**Death of Sister Kenny.**—Sister Elizabeth Kenny, the Australian nurse who became internationally known for her care of poliomyelitis patients, died Nov. 30, 1952, at her home in Toowoomba, Queensland, aged 66, of cerebral thrombosis and pneumonia.

**Director General of WHO Resigns.**—Dr. Brock Chisholm, Geneva, Switzerland, has announced his decision to retire as director-general of the United Nations World Health Organization next July 21, after directing the organization's work since its inception in 1946. His successor will be appointed by the annual assembly in May.

**Publishers Add Medical Book Department.**—Little, Brown and Company, Boston, have announced the formation of a medical book department under the management of Mr. Theodore A. Phillips, formerly vice-president of the Blakiston Company, and previously vice-president and director of J. B. Lippincott Company and sales manager of W. B. Saunders Company.

**Heart Association Publishes Another New Journal.**—*Circulation Research,* a bimonthly journal issued by the American Heart Association, scheduled for January publication, will be edited by Dr. Carl J. Wiggers, professor of physiology, Western Reserve University School of Medicine, Cleveland, with Robert S. Alexander, Ph.D., associate professor of physiology at the same institution, as assistant editor. *Circulation,* which is in its third year of publication, will continue as a separate journal under the editorship of Dr. Thomas M. McMillan, Philadelphia. It will concentrate more fully on clinical problems and applied research, as distinguished from fundamental research in the cardiovascular field. In addition to original papers on fundamental research, editorials on appropriate subjects and short preliminary reports on research in progress will be included in the new periodical, which will have a format similar to that of *Circulation.* Each volume will consist of about 600 pages.

**Pan American Cruise-Congress.**—The Pan American Medical Association has scheduled its eighth international cruise-congress to South America and the West Indies aboard the S. S. Nieuw Amsterdam, sailing from New York Jan 7 and returning Jan. 19. Scientific sessions will be held each morning while the ship is at sea. Registration fee is $25 for each passenger, payable to the Pan American Medical Association. The American Express Travel Company will handle all reservations, subject to the approval of the association. Information may be obtained from the Pan American Medical Association, Executive Offices, 745 Fifth Ave., New York 22.

**Nurses Plan Work Conferences on Poliomyelitis.**—The Nursing Advisory Services for Orthopedics and Poliomyelitis of the National League for Nursing have announced plans to participate in a series of 12 work conferences on the nursing care of poliomyelitis patients, to be held throughout the country in February, March, and April. The purpose of the conferences is to help nurses who are responsible for nursing services, administration of poliomyelitis units, and home care programs, and representatives of nursing education to incorporate the newer methods and trends in their total programs of nursing in the home, hospital, or school. Attendance during the entire conference will be limited to key personnel in hospitals, schools of nursing, and public health agencies; but the last two days of each conference will be open to directors of nursing services and directors of nursing education programs not present during the early part of the conference and to hospital administrators, so that the total field of nursing for patients with poliomyelitis may be carefully explored and planned.

**Society News.**—At its recent meeting in Chicago the American Academy of Dermatology and Syphilology elected Dr. Michael H. Ebert, of Chicago, president, and Dr. Maurice J. Costello, New York, vice-president, and reelected Dr. John E. Rauschkolb, Cleveland, secretary-treasurer.——At its annual meeting in Chicago the American Academy of Obstetrics and Gynecology installed Dr. Robert A. Kimbrough Jr., Philadelphia, as president and named Dr. F. Bayard Carter, Durham, N. C., president-elect; Dr. C. Paul Hodgkinson, Detroit, secretary; Dr. Charles D. Kimball, Seattle, assistant secretary; and Dr. Joe Vincent Meigs, Boston, second vice-president. Drs. Howard C. Stearns, Portland, Ore., and Herbert E. Schmitz, Chicago, were reelected first vice-president and treasurer, respectively.——At its annual meeting the Association of American Medical Colleges chose as president, Dr. Ward Darley, vice-president of Colorado University, Denver; as vice-president, Dr. John Z. Bowers, dean of the University of Utah College of Medicine, Salt Lake City; as secretary, Dr. Dean F. Smiley, Chicago; and as treasurer, Dr. John B. Youmans, dean, Vanderbilt University School of Medicine, Nashville, Tenn. Dr. Stanley E. Dorst, dean of the University of Cincinnati College of Medicine, was named president-elect.——At its annual session in Denver, the American Association of Medical Clinics elected the following officers for the coming year: Dr. Clair L. Stealy, San Diego, Calif., president; Dr. Wayne Gordon, Billings, Mont., vice-president and president-elect; and Dr. Arthur H. Griep, Evansville, Ind., secretary-treasurer. The next meeting of the association will be held in Chicago, in the fall of 1953.——At the annual meeting of the American Radium Society of Chicago, the following officers were elected: president, Dr. Howard B. Hunt, Omaha; president-elect, Edith H. Quimby, D.Sc., New York; first vice-president, Dr. Wendell G. Scott, St. Louis; second vice-president, Dr. James E. Breed, Chicago; secretary, Dr. John E. Wirth (reelected), Pasadena, Calif.; and treasurer, Dr. Grant T. Beckstrand (reelected), Long Beach, Calif. The 35th annual meeting of the society will be held in St. Louis, April 19-22.

## FOREIGN

**Yellow Fever Reported in Colombia.**—According to the U. S. Public Health Service, a fatal case of jungle yellow fever has been reported in La Dorada, Colombia. The patient, infected Nov. 18, 1952, died Nov. 22.

**Britain's Cancer Fatalities Doubled in Ten Years.**—According to the annual British Registrar General's statistical review for 1950, Britain's death toll from cancer has doubled since 1940 and has accounted for 17% of all deaths recorded in England

and Wales for 1950. Cancer killed 85,270 persons, or 1 out of every 3,200 population in 1950. The over-all death rate was 11.6 per 1,000 population compared with 11.7 in 1949. Deaths from tuberculosis totaled 15,900, compared with 20,000 for the previous year. Among 17,700 listed cases of acute poliomyelitis there were 755 deaths or slightly less than 10%. Improvement in the general death rate was noted in every age group except those over 75, the greatest improvement being among children under 4 years.

# EXAMINATIONS AND LICENSURE

## BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 23-25. Sec., Dr. D. G. Gill, 537 Dexter Ave., Montgomery.

ALASKA:* *Examination.* Juneau, March 3. On application in other towns where there are board members. *Reciprocity.* On application. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARIZONA:* *Examination.* Phoenix, Jan. 20-22. *Reciprocity.* Phoenix, Jan. 24. Sec., Dr. J. H. Patterson, 316 W. McDowell Road, Phoenix.

ARKANSAS:* *Homeopathic. Examination.* Little Rock, April 6. Sec., Dr. Carl S. Bungart, 105 North 14th St., Ft. Smith. *Eclectic.* Little Rock, June 4-5. Sec., Dr. Frank C. Smith, 2301 Broadway, Little Rock.

COLORADO:* *Examination.* Denver, Jan. 13-16. Exec. Sec., Mrs. B. H. Hudgens, 831 Republic Bldg., Denver.

CONNECTICUT:* *Medical.* Hartford, March 10-11. Sec., Dr. Creighton Barker, 160 St. Ronan St., New Haven. *Homeopathic.* Derby, March 10-11. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

DELAWARE: *Examination.* Dover, Jan. 13-15. *Reciprocity.* Dover, Jan. 22. Sec., Dr. J. S. McDaniel, 229 South State St., Dover.

FLORIDA:* Jacksonville, June 28-30. Sec., Dr. Homer Pearson, 701 Dupont Bldg., Miami.

GEORGIA: *Examination.* Atlanta and Augusta, June. *Reciprocity.* Atlanta, June. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. Austin W. Matthis, Agana.

HAWAII: Honolulu, Jan. 12-14. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

IDAHO: Boise, Jan. 12-14. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

ILLINOIS: Chicago, Jan. 27-29. Supt. of Regis., Mr. Charles F. Kervin, Capitol Bldg., Springfield.

INDIANA: *Examination.* Indianapolis, June 23-25. Ex. Sec., Miss Ruth V. Kirk, 538 K of P Bldg., Indianapolis.

MAINE: Portland, March 10-11. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MASSACHUSETTS: *Examination.* Boston, Jan. 13-16. Sec., Dr Robert C. Cochrane, Room 37, State House, Boston.

MINNESOTA:* Minneapolis, Jan. 20-22. Sec., Dr. J. F. Du Bois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSOURI: *Examination.* Jefferson City, Feb. 19-20. Exec. Sec., Mr. John A. Hailey, Box 4, State Capitol Bldg., Jefferson City.

MONTANA: *Examination.* Helena, April 7-8. *Reciprocity.* Helena, April 6. Sec., Dr. S. A. Cooney, 7 West 6th Ave., Helena.

NEBRASKA:* *Examination.* Omaha, June 1953. Director, Mr. Husted K. Watson, Room 1009 State Capitol Bldg., Lincoln 9.

NEVADA:* Carson City, Feb. 2. Dr. George H. Ross, 112 North Curry St., Carson City.

NEW JERSEY: Trenton, June 16-19. Sec., Dr. Earl S. Hallinger, 28 West State St., Trenton.

NEW MEXICO:* Santa Fe, April 13-14. Sec., Dr. R. C. Derbyshire, 227 E. Palace Ave., Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 27-30. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany 7.

NORTH CAROLINA. *Reciprocity.* Winston Salem, Jan. 19. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, Jan. 7-9. *Reciprocity.* Grand Forks, Jan. 10. Sec., Dr. C. J. Glaspel, Grafton,

OKLAHOMA:* *Examination.* Oklahoma City, June 10-11. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Examination.* Portland, Jan. 5-6. *Reciprocity.* Portland, Jan. 16-17. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

PENNSYLVANIA: *Examination.* Philadelphia, Jan. 12-15. Acting Sec., Mrs. Marguerite G. Steiner, Box 911, Harrisburg.

RHODE ISLAND:* *Examination.* Providence, Jan. 8-9. Administrator, Division of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: *Examination.* Columbia, Feb. 3. Sec., Mr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA:* Sioux Falls, Jan. 20-21. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

TEXAS:* Fort Worth, June 22-24. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Ft. Worth 2.

UTAH: *Examination.* Salt Lake City, July. Asst. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City.

VERMONT: *Examination.* Burlington, Jan. 29-31. Sec., Dr. F. J. Lawliss, Richford.

WASHINGTON:* *Examination.* Seattle, Jan. 25-28. Sec., Mr. Edward C. Dohm, Department of Licenses, Olympia.

WEST VIRGINIA: Charleston, Jan. 12-14. Sec., Dr. N. H. Dyer, State Office Bldg., No. 3, Charleston 5.

WISCONSIN: *Examination.* Madison, January 13-15. Sec., Dr. A. G. Koehler, 46 Washington Blvd., Oshkosh.

WYOMING: *Examination.* Cheyenne, Feb. 2. Examinations are regularly scheduled the first Monday of February, June and October of each year. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

## BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination.* On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

ARKANSAS: *Examination.* Little Rock, May 5-6. Sec., Mr. Louis E. Gebauer, 1002 Donaghey Bldg., Little Rock.

COLORADO: Denver, March 4-5. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

FLORIDA: *Examination.* Gainesville, June 6. Sec., Mr. M. W. Emmel, Box 340, University of Florida, Gainesville.

IOWA: Des Moines, Jan. 13. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.

MICHIGAN: Detroit and Ann Arbor, Feb. 13-14. Sec., Mrs. Ann Baker, 423 W. Michigan Ave., Lansing.

MINNESOTA: Minneapolis, Jan. 6-7. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: Omaha, Jan. 13-14. Sec., Mr. Husted K. Watson, Room 1009 State Capitol Bldg., Lincoln 9.

NEVADA: *Examination.* Reno, Jan. 6. Sec., Mr. Frank Richardson, University of Nevada, Reno.

NEW MEXICO: *Examination.* Santa Fe, March 15. Sec., Mrs. Marguerite Cantrell, P. O. Box 1592, Santa Fe.

OKLAHOMA: Oklahoma City, April 3. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, March 7. Sec., Dr. Charles D. Byrne, University of Oregon, Eugene.

RHODE ISLAND: *Examination.* Providence, Feb. 11. Administrator, Division of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

TENNESSEE: *Examination.* Memphis, Dec. 31-Jan. 1. Sec., Dr. O. W. Hyman, 874 Union Ave., Memphis.

TEXAS: *Examination.* Dallas and Galveston, April. Sec., Bro. Raphael Wilson, 407 Perry Brooks Bldg., Austin.

WASHINGTON: *Examination.* Seattle, Jan. 21-22. Sec., Mr. Edward C. Dohm, Department of Licenses, Olympia.

* Basic Science Certificate required.

# MEETINGS

**AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.**

**1953 Annual Session, New York, June 1-5.**

**1953 Clinical Session, St. Louis, Dec. 1-4.**

**1954 Annual Session, San Francisco, June 21-25.**

**1954 Clinical Session, Miami, Florida, Nov. 30-Dec. 3.**

ANNUAL CONGRESS ON INDUSTRIAL HEALTH, Drake Hotel, Chicago, Jan. 20-22. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago 10, Secretary.

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE, Palmer House, Chicago, Feb. 9-10. Dr. Donald G. Anderson, 535 North Dearborn St., Chicago, Secretary.

NATIONAL CONFERENCE ON RURAL HEALTH, Roanoke Hotel, Roanoke, Va., Feb. 27-28. Mrs. Arline Hibbard, 535 N. Dearborn St., Chicago 10, Secretary.

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AMERICAN ACADEMY OF ALLERGY, Statler Hotel, Boston, Feb. 26-28. Dr. Ben Z. Rappaport, 55 East Washington St., Chicago, Secretary.

AMERICAN ACADEMY OF FORENSIC SCIENCES, Drake Hotel, Chicago, Feb. 26-28. Prof. Ralph F. Turner, Michigan State College, Dept. of Police Administration, East Lansing, Mich., Secretary.

AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS, Palmer House, Chicago, Jan. 24-29. Dr. John R. Norcross, 122 South Michigan Avenue, Chicago 3, Secretary.

AMERICAN COLLEGE OF RADIOLOGY, Palmer House, Chicago, Feb. 6. Mr. William C. Stronach, 20 North Wacker Drive, Chicago 6, Executive Secretary.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY:

EASTERN SECTION, Hotel Syracuse, Syracuse, N. Y., Jan. 7. Dr. Francis W. Davison, Danville, Pa., Chairman.

MIDDLE SECTION, Drake Hotel, Chicago, Jan. 19. Dr. Ralph J. McQuiston, 20 North Meridian St., Indianapolis 4, Chairman.

SOUTHERN SECTION, Andrew Jackson Hotel, Nashville, Tenn., Jan. 12. Dr. Lester A. Brown, 490 Peachtree St., N.E., Atlanta 3, Ga., Chairman.

WESTERN SECTION, Elks Club, Los Angeles, Jan. 24. Dr. Howard P. House, 1136 West Sixth St., Los Angeles 14, Chairman.

AMERICAN ORTHOPSYCHIATRIC ASSOCIATION, Hotel Statler, Cleveland, Feb. 23-25. Dr. Exie E. Welsch, 303 Lexington Ave., New York 16, Secretary.

AMERICAN PROTESTANT HOSPITAL ASSOCIATION, Palmer House, Chicago, Feb. 10-13. Mr. Albert G. Hahn, Protestant Deaconess Hospital, Evansville, Ind., Executive Secretary.

INTERNATIONAL POST-GRADUATE MEDICAL ASSEMBLY OF SOUTHWEST TEXAS, Municipal Auditorium, San Antonio, Texas, Jan. 27-29. Dr. John M. Smith Jr., P. O. Box 2445, San Antonio 6, Texas, Secretary.

NORTHWEST SOCIETY FOR CLINICAL RESEARCH, Seattle, Jan. 16-17. Dr. Arthur L. Rogers, 1216 S.W. Yamhill St., Portland 5, Ore., Secretary.

REGIONAL MEETINGS, AMERICAN COLLEGE OF PHYSICIANS:

EASTERN PENNSYLVANIA, Philadelphia, Jan. 16. Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.

COLORADO, Denver, February 17, Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.

DELAWARE, Wilmington, Feb. 27. Mr. E. R. Loveland, 4200 Pine St., Philadelphia, Executive Secretary.

VIRGINIA, Norfolk, Feb. 26. Mr. E. R. Loveland, 4200 Pine St., Philadelphia, Executive Secretary.

SECTIONAL MEETINGS, AMERICAN COLLEGE OF SURGEONS:

CINCINNATI, The Netherland Plaza, Jan. 19-21. Dr. M. M. Zinninger, Cincinnati General Hospital, Cincinnati 29, Chairman.

ATLANTA, GA., The Atlanta Biltmore, Feb. 23-24. Dr. William G. Hamm, 384 Peachtree St. N.E., Atlanta, Chairman.

SOCIETY OF UNIVERSITY SURGEONS, Washington University, St. Louis, Feb. 12-14. Dr. Clarence Dennis, Kings County Hospital, Brooklyn, N. Y., Secretary.

U. S. CHAPTER, INTERNATIONAL COLLEGE OF SURGEONS, SURGICAL DIVISION MEETINGS:

TRI-STATE ASSEMBLY OF TEXAS, Arkansas and Oklahoma, Adolphus Hotel, Dallas, Texas, Feb. 5-7. Dr. Curtice Rosser, 710 Medical Arts Bldg., Dallas, Texas, Chairman.

PENNSYLVANIA AND SURROUNDING STATES, Bellevue-Stratford Hotel, Philadelphia, Feb. 13-14. Dr. Moses Behrend, 225 South 17th St., Philadelphia, Chairman.

WESTERN SOCIETY FOR CLINICAL RESEARCH, Carmel, Calif., Jan. 30-31. Dr. Herbert N. Hultgren, Stanford Hospital, San Francisco 15, Secretary.

**INTERNATIONAL**

CONGRESS OF INTERNATIONAL LEAGUE AGAINST RHEUMATISM, Geneva and Zurich, Switzerland, Aug. 24-29, 1953. For information write: Dr. W. Tegner, The London Hospital, London E.1, England.

CONGRESS OF THE INTERNATIONAL SOCIETY OF SURGERY, Lisbon, Portugal, Sept. 15-20, 1953. Dr. L. Dejardin, 141, rue Belliard, Brussels, Belgium, General Secretary.

INTER-AMERICAN SESSION, AMERICAN College of Surgeons, Paulista Medical Association Bldg., Sao Paulo, Brazil, Feb. 9-12, 1953. Dr. Moacyr Eyck Alvaro, 1151 Conselacao, Sao Paulo, Brazil, Chairman.

INTERNATIONAL CONGRESS OF AUDIOLOGY, Groningen, Netherlands, June 5-6, 1953. Dr. Gunnar Holmgren, Strandvagen 5A, Stockholm, Sweden, President.

INTERNATIONAL CONGRESS OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY, Boston, Mass., U. S. A., Aug. 18-21, 1953. Dr. Robert S. Schwab, Massachusetts General Hospital, Boston 14, Mass., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS FOR HISTORY OF SCIENCE, Jerusalem, Israel, August 3-7, 1953. Prof. F. S. Bodenheimer, Hebrew University, Jerusalem, Israel, President.

INTERNATIONAL CONGRESS ON MEDICAL LIBRARIANSHIP, London, England, July 20-25, 1953. Mr. W. R. LeFanu, % London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1, England, Chairman.

INTERNATIONAL CONGRESS OF MICROBIOLOGY, Rome, Italy, Sept. 6-12, 1953. For information write: Dr. V. Puntoni, Citta Universitaria, Rome, Italy.

INTERNATIONAL CONGRESS OF OTORHINOLARYNGOLOGY, Amsterdam, Netherlands, June 8-15, 1953. Dr. W. H. Struben, J. J. Viottastraat 1, Amsterdam, Netherlands, Secretary.

INTERNATIONAL CONGRESS OF PAEDIATRICS, Havana, Cuba, Oct. 12-17, 1953. Prof. Felix Hurtado, 5a Avenue 124, Miramar, Havana, Cuba, President.

INTERNATIONAL CONGRESS OF RADIO-BIOLOGY, Copenhagen, Denmark, July 14-25, 1953. Prof. Flemming Norgaard, Oster Voldgade 10, Copenhagen K, Denmark, Secretary General.

INTERNATIONAL CONGRESS OF RADIOLOGY, Copenhagen, Denmark, July 19-25, 1953. Professor Flemming Norgaard, 10 Oster Voldgade, Copenhagen K., Denmark, Secretary General.

INTERNATIONAL CONGRESS OF THALASSOTHERAPY, Dubrovnick, Yugoslavia, May 17-25, 1953. Prof. C. Plavaic, Mavrodne Republick 51, Belgrade, Yugoslavia, Secretary General.

INTERNATIONAL CONGRESSES OF TROPICAL MEDICINE AND MALARIA, Istanbul, Turkey, Aug. 28-Sept. 4, 1953. Professor Dr. Ihsan Sükrü Aksel, Tunel Meydam, Beyoglu, Istanbul, Turkey, General Secretary.

INTERNATIONAL FERTILITY ASSOCIATION, New York, N. Y., U. S. A., May 25-31, 1953. Dr. Abner I. Weisman, 1160 Fifth Avenue, New York 29, N. Y., U. S. A., Associate Secretary General.

INTERNATIONAL HOSPITAL CONGRESS, London, England, May 25-30, 1953. Capt. J. E. Stone, 10 Old Jewry, London, EC2, England, Hon. Secretary.

INTERNATIONAL LEPROSY CONGRESS, Madrid, Spain, Oct. 3-10, 1953. Dr. Felix Contreras, Moreto 15, Madrid, Spain, Secretary.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Montreal, Canada, Aug. 31-Sept. 4, 1953. Dr. A. S. V. Burgen, Dept. of Physiology, McGill University, Montreal, Canada, Secretary.

INTERNATIONAL PSYCHO-ANALYTICAL CONGRESS, Bedford College, Regent's Park, London N.W.1, England, July 26-30. Dr. Ruth S. Eissler, 285 Central Park West, New York 24, N. Y., Hon. Secretary.

INTERNATIONAL VETERINARY CONGRESS, Stockholm, Sweden, Aug. 9-15, 1953. Prof. Axel Isaksson, Institute of Veterinary Medicine, Stockholm 50, Sweden, Secretary.

PAN AMERICAN CONGRESS OF THE MEDICAL PRESS, Buenos Aires, Argentine, July 12-16, 1953. Secretaria del Congress, 763 Uriburu, Buenos Aires, Argentine.

PAN AMERICAN MEDICAL ASSOCIATION, International Medical Cruise Congress, S. S. Nieuw Amsterdam, Jan. 7-19. Executive Offices, 745 Fifth Ave., New York 22, N. Y.

WORLD CONFERENCE ON MEDICAL EDUCATION, British Medical Association House, Tavistock Square, W.C.1, London, England, Aug. 24-29, 1953. Secretariat: World Medical Association, 2 East 103d St., New York 29, N. Y., U. S. A.

WORLD CONGRESS OF THE WORLD CONFEDERATION FOR PHYSICAL THERAPY, London, England, Sept. 7-12, 1953. Miss M. J. Neilson, Chartered Society of Physiotherapy, Tavistock House, South, Tavistock Square, London, W.C 1, England, Secretary.

WORLD MEDICAL ASSOCIATION, Amsterdam, Holland, Aug. 31-Sept. 6, 1953. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary-General.

# DEATHS

**Tynes, Achilles Lyons** ⊕ Staunton, Va.; born in Tazewell, Va., March 11, 1873; University College of Medicine, Richmond, 1898; charter member, past president, and secretary of the Augusta County Medical Society; served as a vice-president of the Medical Society of Virginia and president of the Medical College of Virginia Alumni Association; served during World War I; formerly city health officer; an Associate Fellow of the American Medical Association; past president of the board of visitors and for many years member of the board of trustees of the Hampden-Sydney College, which awarded him its highest honor, the Algernon Sidney Memorial medal for distinguished service; died in McGuire General Hospital, Richmond, Oct. 26, aged 79, of coronary thrombosis.

**Lavoie, Aurel Gilbert** ⊕ Springfield, Mass.; Tufts College Medical School, Boston, 1933; certified by the National Board of Medical Examiners; member of the New England Obstetrical and Gynecological Society; fellow of the International College of Surgeons and the American College of Surgeons; served during World War II; affiliated with Mercy and Wesson Memorial hospitals; surgeon, outpatient department, Springfield Hospital; consulting surgeon, Mary Lane Hospital, Ware, and Monson State Hospital in Palmer; died in Phillips House, Massachusetts General Hospital, Boston, Oct. 26, aged 45, of uremia, hypertension, and congestive heart failure.

**Plummer, Samuel Craig** ⊕ Boulder, Colo.; Chicago Medical College, 1886; member of the House of Delegates of the American Medical Association in 1904; member of the Illinois State Medical Society, American Surgical Association, and Western Surgical Association; fellow of the American College of Surgeons; served during World War I; at one time practiced in Chicago, where he was professor of surgery emeritus at his alma mater, now known as Northwestern University Medical School, and senior surgeon emeritus at St. Luke's Hospital; retired chief surgeon, Chicago, Rock Island, and Pacific Railway; died Nov. 21, aged 87, of cardiovascular failure.

**Beck, Richmond James** ⊕ Lyons, N. J.; born in Stevens Point, Wis., April 7, 1896; George Washington University School of Medicine, Washington, D. C., 1921; specialist certified by the American Board of Psychiatry and Neurology; fellow of the American Psychiatric Association and the Medical Society of the State of New York; served during World Wars I and II; received a commendation ribbon "for distinguished service in line of his profession as psychiatrist and embarkation-debarkation officer aboard the *U.S.S. Solace* from November 1943 to July 1945"; chief of physical medicine at the Veterans Administration Hospital; died in a hotel in New York Nov. 11, aged 56.

**Curry, Marcus Albert** ⊕ Greystone Park, N. J.; Albany (N. Y.) Medical College, 1904; an Associate Fellow of the American Medical Association; life member of the American Psychiatric Association; member of the Association for Research in Nervous and Mental Diseases; life member and past president of the Morris County Medical Society; charter member of the New Jersey Neuropsychiatric Association; specialist certified by the American Board of Psychiatry and Neurology; for many years superintendent of the New Jersey State Hospital; died Nov. 11, aged 74, of pulmonary embolism.

**Adams, Frederick Cecil** ⊕ Klamath Falls, Ore.; University of Oregon Medical School, Portland, 1927; affiliated with Klamath Valley and Hillside hospitals; died Sept. 4, aged 54, of coronary occlusion.

**Albright, Henry Richard,** Kansas City, Mo.; University Medical College of Kansas City, 1895; died Nov. 18, aged 81, of arteriosclerotic heart disease.

**Alger, George Lavorious,** Saginaw, Mich.; Saginaw Valley Medical College, 1901; served during World War I; died Aug. 6, aged 76, of myocardial infarction.

**Basquin, Fred S.,** Chardon, Ohio; Cleveland Homeopathic Medical College, 1898; died Oct. 21, aged 79, of coronary occlusion.

**Baynham, Charles William,** Dallas, Texas; (licensed in Arkansas in 1903 and Oklahoma in 1909); died Nov. 10, aged 82, of arteriosclerosis.

**Beals, Arthur Loring** ⊕ Charlton, Mass.; Columbia University College of Physicians and Surgeons, New York, 1895; for many years practiced in Brockton, where he was city physician, school physician, and associated with Brockton Hospital; died Oct. 20, aged 83, of arteriosclerotic heart disease.

**Belanger, Henri,** River Rouge, Mich.; Detroit College of Medicine, 1894; for many years health officer and member of the board of education; served as senior consultant to the Delray General Hospital in Detroit; died Nov. 1, aged 80.

**Berndt, Daniel Albert** ⊕ Portsmouth, Ohio; College of Physicians and Surgeons, Baltimore, 1896; fellow of the American College of Surgeons; past president of the Hempstead Academy of Medicine; served as president of the Norfolk & Western Railway Surgeons Association; physician and surgeon for the Norfolk & Western Railway; affiliated with Mercy Hospital and Portsmouth General Hospital, where he died Nov. 3, aged 78.

**Best, Jesse Carnes** ⊕ Oklahoma City, Okla.; Southern Methodist University Medical Department, Dallas, 1912; died Nov. 4, aged 64.

**Blessing, Robert** ⊕ Fort Lauderdale, Fla.; Northwestern University Medical School, Chicago, 1921; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; affiliated with Broward General Hospital, where he died Oct. 29, aged 56, of coronary thrombosis.

**Boisseau, James Gordon** ⊕ Richmond, Va.; Medical College of Virginia, Richmond, 1914; served during World War I; died Nov. 8, aged 63, of coronary thrombosis.

**Broberg, John Aaron,** Blue Earth, Minn.; University of Michigan Medical School, Ann Arbor, 1892; for many years health officer; died Oct. 13, aged 90, of uremia and hypertrophy of the prostate.

**Brown, Richard J.** ⊕ Sutton, W. Va.; Kentucky School of Medicine, Louisville, 1896; College of Physicians and Surgeons, Baltimore, 1908; died in Sutton General Hospital Nov. 13, aged 83, of gastric ulcer.

**Bullard, John Bunyan,** Richmond, Va.; North Carolina Medical College, Charlotte, 1917; served during World War I; assistant to the medical director of the city public school system; formerly on the faculty of the Medical College of Virginia; affiliated with Grace Hospital, Retreat for the Sick, Stuart Circle Hospital, and Sheltering Arms Hospital; died Oct. 29, aged 59, of coronary thrombosis.

**Bush, Daniel P.,** Bradenton, Fla.; George Washington University School of Medicine, Washington, D. C., 1905; died Nov. 18, aged 83.

**Cahill, John Andrew,** Brooklyn; University and Bellevue Hospital Medical College, New York, 1913; served during World War I; medical superintendent of the Kingston Avenue Hospital; died Nov. 12, aged 62.

**Caine, Jesse Edward,** Tarboro, N. C.; Leonard Medical School, Raleigh, 1912; died Sept. 12, aged 73, of hemorrhage from peptic ulcer.

**Carruth, Robert McGimsey** ⊕ New Roads, La.; College of Physicians and Surgeons, Baltimore, 1880; served as a member of the state board of charities and corrections and as local surgeon for Texas and Pacific Railway; died Nov. 6, aged 96.

**Chittick, Archibald Golding** ⊕ Frankfort, Ind.; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1907; member of the Radiological Society of North America; served during World War I; died in the Veterans Administration Hospital, Indianapolis, Oct. 26, aged 69, of myocardial infarct.

⊕ Indicates Member of the American Medical Association.

**Clark, Burton O.,** Hampton, Va.; Ensworth Medical College, St. Joseph, Mo., 1907; died in the Veterans Administration Hospital Aug. 7, aged 75, of cerebral hemorrhage.

**Congdon, John Bowman** ✠ Albany, N. Y.; Albany Medical College, 1902; fellow of the American College of Surgeons; member of the Industrial Medical Association; served on the staffs of the Memorial and St. Peter's hospitals; died in Rutland, Vt., Nov. 12, aged 76.

**Cook, Harrison Irving** ✠ New York City; University and Bellevue Hospital Medical College, New York, 1911; died in Wickersham Hospital Sept. 11, aged 63, of cancer.

**Copeland, William Flournoy** ✠ Lynnville, Tenn.; University of Nashville Medical Department, 1904; served as mayor of Lynnville; died in Vanderbilt University Hospital, Nashville, Oct. 30, aged 74.

**Crabtree, Samuel Alonzo,** Martinsville, Ohio; Miami Medical College, Cincinnati, 1901; died in Springfield Oct. 30, aged 83, of tuberculosis.

**Craven, Thomas** ✠ Huntersville, N. C.; Jefferson Medical College of Philadelphia, 1917; served during World War II; died Aug. 10, aged 63, of coronary occlusion.

**Deitz, George Washington** ✠ Philadelphia; Medico-Chirurgical College of Philadelphia, 1908; for many years affiliated with Frankford Hospital, where he was past president of the staff, and consultant at Friends Hospital; at various times associated with St. Christopher's, Stetson, and Northeastern hospitals; died in St. Petersburg, Fla., Nov. 7, aged 68, of acute cardiac failure.

**Deppe, Edwin Fay** ✠ Seattle; New York Homeopathic Medical College and Flower Hospital, New York, 1931; served during World War II; on the staff of the King County Hospital; died in Veterans Administration Hospital Nov. 8, aged 47, of pulmonary edema.

**DeWitt, Paul** ✠ Madison, Tenn.; Vanderbilt University School of Medicine, Nashville, 1905; at one time on the faculty of the dental department of his alma mater; fellow of the American College of Surgeons; served during World War I; affiliated with Mid-State Baptist and Nashville General hospitals; died Nov. 6, aged 74, of coronary thrombosis.

**Douglass, John** ✠ Birmingham, Ala.; Birmingham Medical College, 1900; died Nov. 1, aged 76.

**Dunn, Ernest Alexander Allen** ✠ Bethesda, Md.; National University Medical Department, Washington, D. C., 1898; died Nov. 8, aged 80, of cerebral thrombosis.

**Dyer, Henry Lathrop** ✠ Lieutenant, U. S. Navy, retired, Gorham, N. H.; Medical School of Maine, Portland, 1918; retired May 6, 1921, for incapacity resulting from an incident of the service; member of the American College of Chest Physicians and the American Trudeau Society; served on the staff of St. Louis Hospital in Berlin; died Oct. 10, aged 56, of coronary occlusion and pulmonary tuberculosis.

**Elder, John Minford** ✠ Niles, Ohio; Miami Medical College, Cincinnati, 1899; formerly health officer of Mineral Ridge; retired in 1951 as president of the Home Federal Savings & Loan Association; affiliated with Trumbull Memorial Hospital in Warren; died Oct. 22, aged 80, of bronchopneumonia.

**Emerson, Mark Lewis** ✠ Oakland, Calif.; Medical Department of the University of California, San Francisco, 1899; fellow of the American College of Surgeons; past president of the Alameda County Medical Society; county coroner; formerly health officer of Oakland; for many years affiliated with Fairmont Hospital of Alameda County and Samuel Merritt Hospital; died Nov. 11, aged 80.

**Fox, George Raymond** ✠ East Providence, R. I.; Georgetown University School of Medicine, Washington, D. C., 1927; member of the Industrial Medical Association; fellow of the American College of Surgeons; served as president of the Pawtucket Medical Association and as treasurer of the Rhode Island Medical Society; affiliated with State Sanatorium, Wallum Lake, Roger Williams General Hospital and St. Joseph's Hospital in Providence, and the Memorial Hospital in Pawtucket, where he died Oct. 25, aged 49.

**Fryar, Claude Henry,** Carolina Beach, N. C.; Medical College of Virginia, Richmond, 1918; died Aug. 10, aged 58, of coronary occlusion and hypertension.

**Gallagher, Joseph Francis Howard** ✠ Nashville, Tenn.; University of Nashville Medical Department, 1906; assistant professor of clinical gynecology at Vanderbilt University School of Medicine; past president of the Tennessee Cancer Society; formerly secretary of the Tennessee State Medical Association; affiliated with St. Thomas and Nashville General hospitals; died Oct. 21, aged 68, of cerebral hemorrhage.

**Gardner, George Rolland,** Ashville, Ohio; Ohio Medical University, Columbus, 1897; died in Grant Hospital, Columbus, Oct. 30, aged 79.

**Glenn, Robert Alexander** ✠ Oakland, Calif.; University of Pennsylvania School of Medicine, Philadelphia, 1911; specialist certified by the American Board of Pathology; member of the College of American Pathologists and the American Society of Clinical Pathologists; affiliated with Samuel Merritt Hospital; died Nov. 13, aged 65, of nephrosis with uremia, arteriosclerosis, and hypertension.

**Golding, Harold Horton** ✠ Peekskill, N. Y.; Cornell University Medical College, New York, 1911; served during World War I; health officer of Peekskill; formerly director of Peekskill Savings Bank; affiliated with Peekskill Hospital; died in Neurological Institute, New York, Nov. 8, aged 65, of coronary occlusion following an operation for brain tumor.

**Grady, William Patrick** ✠ Bethesda, Md.; Medico-Chirurgical College of Philadelphia, 1902; member of the Medical Society of the State of Pennsylvania; for many years affiliated with St. Mary's Hospital; in 1939 received the honorary degree of doctor of laws from St. Joseph's College, Philadelphia; died Oct. 20, aged 76, of pulmonary embolism and myocardial infarction.

**Grant, Sylvia** ✠ Clarksburg, W. Va.; University of Maryland School of Medicine, College of Physicians and Surgeons, Baltimore, 1924; died in Bridgeport Nov. 9, aged 61, of cardiac failure.

**Graves, Gaylor Willis** ✠ Jackson Heights, N. Y.; Cornell University Medical College New York, 1908; clinical professor of pediatrics at New York University College of Medicine; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; affiliated with Bellevue Hospital in New York; co-author with Dr. C. G. Kerley of "Practice of Pediatrics"; died Nov. 8, aged 68.

**Guinea, William Emmett** ✠ Chicago; Chicago College of Medicine and Surgery, 1916; for many years on the staff of the Little Company of Mary Hospital, where he died Nov. 22, aged 60, of heart disease.

**Hall, Charles W.,** Burdick, Kan.; Ensworth Medical College, St. Joseph, Mo., 1907; died Oct. 20, aged 80, of a heart attack.

**Hall, Kenneth Roger** ✠ Gadsden, Ala.; Meharry Medical College, Nashville, Tenn., 1947; died Aug. 3, aged 30, of a fractured skull received in an automobile accident.

**Haralson, Charles Herndon** ✠ Tulsa, Okla.; Atlanta Medical College, 1914; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; past president of the Oklahoma State Medical Association and the Tulsa County Medical Society; served during World War I; affiliated with Hillcrest and St. John's hospitals; died Oct. 29, aged 60, of cerebral thrombosis.

**Harrison, Calvin Linsley,** New Haven, Conn.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1887; served as assistant medical director of the New York Life Insurance Company; died Nov. 2, aged 90.

**Harrison, Emmett Merrick** ✠ Chattanooga, Tenn.; Chattanooga Medical College, 1902; died in Veterans Administration Hospital, Murfreesboro, Aug. 5, aged 71, of heart disease.

**Hawkins, Robert** ✠ Marysville, Kan.; Rush Medical College, Chicago, 1885; died Oct. 25, aged 93, of coronary occlusion.

**Hays, Walter Colquitt** ⊕ Colquitt, Ga.; Atlanta School of Medicine, 1908; died Sept. 13, aged 72, of coronary thrombosis.

**Hobson, Edwin Lafayette Jr.,** State Farm, Va.; University College of Medicine, Richmond, 1895; died Oct. 8, aged 83.

**Holloman, Alfred Leon** ⊕ Savannah, Ga.; Baylor University College of Medicine, Dallas, 1939; fellow of the American College of Surgeons; affiliated with U. S. Public Health Service during World War II; served on the staffs of St. Joseph's and Warren A. Candler hospitals and Georgia Infirmary; consultant in surgery, U. S. Marine Hospital; died Oct. 20, aged 37, of brain tumor.

**Hopkins, Mark Forrest** ⊕ San Jose, Calif.; College of Physicians and Surgeons of San Francisco, 1903; an Associate Fellow of the American Medical Association; died Oct. 28, aged 74.

**Hoskins, Horace Faulkner,** Saluda, Va.; Medical College of Virginia, Richmond, 1908; died in Richmond Aug. 28, aged 72.

**Houston, Thomas D.,** Montpelier, Miss.; University of Nashville (Tenn.) Medical Department, 1906; died Oct. 27, aged 71.

**Jones, Washington Leonidas** ⊕ Youngstown, Ohio; Detroit College of Medicine, 1908; member of the American Academy of General Practice; affiliated with St. Elizabeth Hospital; died Oct. 28, aged 69, of coronary thrombosis.

**Keidel, Victor** ⊕ Fredericksburg, Texas; Jefferson Medical College of Philadelphia, 1906; city health officer; formerly county health officer; medical superintendent and a founder of the Keidel Memorial Hospital, where he died Nov. 10, aged 70.

**Kierulff, George Browning,** Melvern, Kan.; University Medical College of Kansas City, 1907; served as president of the Osage County Medical Society; once mayor of Melvern; died Nov. 14, aged 75, of coronary occlusion.

**Koch, Isidore Martin,** Philadelphia; Medico-Chirurgical College of Philadelphia, 1891; died Oct. 16, aged 81, of anaplastic epidermoid carcinoma of lip, arteriosclerosis and hemiplegia.

**Kuntz, William Manion** ⊕ Millersport, Ohio; Ohio State University College of Medicine, Columbus, 1940; served overseas during World War II; died in Lancaster Fairfield Hospital in Lancaster Nov. 9, aged 36.

**Lamar, James N.,** Bruce, Miss.; University of Nashville (Tenn.) Medical Department, 1900; died Nov. 17, aged 90.

**Lasley, James Mecum,** Greystone Park, N. J.; University of Cincinnati College of Medicine, 1925; member of the American Psychiatric Association; served during World War I; resident, New Jersey State Hospital; died Nov. 5, aged 57.

**McGee, Harry Hand** ⊕ Savannah, Ga.; Medical College of Georgia, Augusta, 1924; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society, Radiological Society of North America, and the American College of Radiology; served during World Wars I and II; died in the Duke University Hospital in Durham, N. C., Nov. 6, aged 51.

**Morford, William Brown** ⊕ Penfield, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1896; member of the Medical Society of the State of New York; died in Bryn Mawr (Pa.) Hospital Nov. 4, aged 78, of gastrointestinal hemorrhage.

**Morgenstern, David M.** ⊕ Richmond Hill, N. Y.; New York Homeopathic Medical College and Flower Hospital, 1928; served during World War II; affiliated with Queens General Hospital, Jamaica, and the Veterans Administration Hospital, where he died Nov. 3, aged 51, of carcinoma of the colon with metastases.

**Norris, Lester Francis,** Madison, Maine; College of Physicians and Surgeons, Baltimore, 1912; school physician for many years and school football physician since 1923; served as assistant physician at Taunton (Mass.) State Hospital, assistant superintendent of Bangor (Me.) State Hospital, house physician at Central Maine General Hospital in Lewiston, and state psychiatrist to the women's reformatory in Skowhegan; died Oct. 30, aged 68.

**Rees, Thomas David,** Idaho Falls, Idaho; Rush Medical College, Chicago, 1912; affiliated with Idaho Falls Latter-Day Saints' Hospital; died Nov. 3, aged 75, of coronary occlusion.

**Richardson, Henry Dee,** Nashville, Tenn.; Meharry Medical College, Nashville, 1921; clinical assistant professor of medicine at his alma mater; died Oct. 29, aged 60.

**Ritchey, Romney Moore,** Surgeon, U. S. Public Health Service, reserve, retired, Millbrae, Calif.; Rush Medical College, Chicago, 1904; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; served during World War I; formerly chief medical officer at United States Penitentiary at Alcatraz; died Nov. 8, aged 76.

**Rose, Bernard** ⊕ Detroit; Detroit College of Medicine and Surgery, 1922; for many years on the courtesy staff of the Grace Hospital, where he died Oct. 27, aged 52, of coronary thrombosis.

**Ruston, Warren Dunn** ⊕ Rockport, Mass.; Harvard Medical School, Boston, 1903; served during World War I; formerly affiliated with Boston City Hospital and Somerville (Mass.) Hospital; died in Chelsea Nov. 6, aged 75.

**Schraff, Raymond Joseph Nicholas** ⊕ Cleveland; Western Reserve University Medical Department, Cleveland, 1919; member of the American Association of Railway Surgeons; served during World War I; on the staff of St. John's Hospital; on the courtesy staffs of the Lakewood, Lutheran, and St. Alexis hospitals; company surgeon for the Erie and New York Central Railroads; consulting surgeon for the Nickel Plate Railroad; charter member of the Cleveland Police Department's medical and surgical consultation board; died Oct. 29, aged 58, of carcinoma of the lung.

**Schroeder, Mary Gritzner** ⊕ Wilmette, Ill.; Rush Medical College, Chicago, 1921; member of the American Psychiatric Association; past president of the Chicago chapter of the Women's Medical National Association; for many years clinical associate in medicine, neurology, and psychiatry at her alma mater; served on the staff of the Elgin (Ill.) State Hospital; died in Evanston Nov. 16, aged 83, of coronary insufficiency and arteriosclerosis.

**Schuler, Russell Philip** ⊕ Kokomo, Ind.; Rush Medical College, Chicago, 1909; affiliated with St. Joseph Memorial Hospital; died Oct. 24, aged 69, of cerebral hemorrhage.

**Schultz, Walter Henry** ⊕ Schleswig, Iowa; Rush Medical College, Chicago, 1900; died Nov. 2, aged 75, of cancer.

**Shinners, Burton Michael** ⊕ Buffalo; Duke University School of Medicine, Durham, N. C., 1936; certified by the National Board of Medical Examiners; specialist certified by the American Board of Psychiatry and Neurology; assistant professor of neurology, University of Buffalo School of Medicine; affiliated with Children's Hospital, Mercy Hospital, and Buffalo General Hospital, where he died Nov. 11, aged 41, of uremia.

**Sloo, Milo Goss** ⊕ Topeka, Kan.; Rush Medical College, Chicago, 1903; affiliated with Stormont-Vail Hospital; died Nov. 4, aged 73, of chronic valvular heart disease.

**Smith, Alan Welch,** Portland, Ore.; College of Physicians and Surgeons, Baltimore, 1895; past president of the state board of health; past president of the Portland City and County Medical Society; served on the city school board; died Nov. 8, aged 81, of cerebral hemorrhage.

**Smith, Ernest Madison** ⊕ Selmer, Tenn.; Memphis (Tenn.) Medical College, 1913; died Oct. 8, aged 63, of carcinoma of the liver.

**Smith, Henry P.,** Hattiesburg, Miss.; Mississippi Medical College, Meridian, 1907; member of the school board in New Augusta; died in Methodist Hospital Nov. 20, aged 76.

**Snyder, George** ⊕ Weston, W. Va.; Eclectic Medical Institute, Cincinnati, 1889; past president of the Lewis County Medical Society; affiliated with City Hospital; died Nov. 4, aged 89, of cerebral hemorrhage.

**Thomas, Delano Charles,** Pittsburgh; Cleveland Homeopathic Medical College, 1903; died in Western Pennsylvania Hospital Oct. 17, aged 74, of heart disease.

**Trach, John M.** ⊕ Fairmont, W. Va.; Illinois Medical College, Chicago, 1900; an Associate Fellow of the American Medical Association; died in the Fairmont General Hospital Oct. 18, aged 77, of coronary thrombosis.

# GOVERNMENT SERVICES

## NAVY

**The Health of the Navy.**—The sick list admission rate among active-duty Navy and Marine Corps personnel during fiscal year 1952 was 357.5 per 1,000 average strength. This means that during the year the equivalent of more than one out of every three persons on active duty were admitted to the sick list, a rate representing an improvement of about 7% over the previous year. Of the total number of persons who were on the sick list, about 45% were admitted to naval hospitals. The remainder were treated in infirmaries, ship sickbays, and, to some extent, in non-naval hospitals. The noneffective rate, which is a measure of the temporary manpower loss due to medical causes, was 19.2 per 1,000 during the fiscal year. This means that, on the average, for every 1,000 persons on duty about 19 were on the sick list every day. This was about 2 per 1,000 lower than in the preceding year, thus saving over one-half million man days, enough manpower to operate a flotilla of destroyers for one year. The incidence rate, a major criterion by which the health of the Navy may be evaluated, relates the frequency of new cases of disease and injuries to the strength exposed. The incidence rates for the last two fiscal years were 449.1 per 1,000 for 1952 as compared to 463.4 per 1,000 for 1951. This decrease was evident for both diseases and injuries.

*Respiratory Disease.*—The incidence rate for acute respiratory infections was 86.4 per 1,000 average strength, almost 18% lower than for the preceding year. As in previous years, the highest rate for these conditions (112.3 per 1,000) was reported by continental stations. This probably is due to the fact that the Navy and Marine Corps training centers are located in continental United States. February was the peak month for acute respiratory infections, with a rate of 190.9 per 1,000, which was almost 30% below that in February, 1951. The decrease in the incidence rate for acute respiratory infections was primarily a reflection of the lowered incidence of the common cold.

*Venereal Disease.*—The incidence rate for venereal disease was 42.2 per 1,000, somewhat lower than during fiscal year 1951. In continental United States the rate remained about the same, 16 per 1,000 average strength. An increase from 85.3 to 88.9 per 1,000 was noted for noncontinental areas. The Pacific fleet had the most marked reduction in venereal disease. The rates for the Atlantic fleet, which were less than half those for the Pacific fleet, also declined, but to a much smaller extent. Gonorrhea accounted for about 75% of the total venereal diseases, chancroid for about 20%, early syphilis about 2%, and other forms of syphilis, as well as lymphogranuloma venereum and granuloma inguinale, for the remainder. The decrease in gonorrhea from 37.0 to 31.3 per 1,000 is largely responsible for the lowered venereal disease rate for the fiscal year.

*Malaria.*—While malaria has been of little importance in the Navy since the end of World War II, the sudden appearance of malaria at the close of the first year of the Korean action prompted increased emphasis on preventive measures. The incidence rate for malaria for fiscal year 1952 was 1.2 per 1,000 average strength, four times as high as in the previous year. Several investigations have indicated that most persons diagnosed as having malaria were marines who had returned from Korea.

*Nervous Disease.*—The incidence rate for mental, psychoneurotic, and personality disorders was 17.1 per 1,000 average strength. In continental United States the rate increased to 23.8 per 1,000 from 18.7 in the preceding year. In noncontinental areas the reverse is true, with the rate declining to 19.2 in 1952 from 23.7 per 1,000 in 1951. For ships the current rate of 5.2 is only slightly higher than the 1951 rate of 4.6 per 1,000. The Korean action has had its effect on the incidence for these conditions in all areas. While the incidence in noncontinental areas was higher than in continental areas during the first year of the Korean action, the prolonged experience of the men in that area and the comparative lull during the current year from the truce negotiations may have been responsible for the lower rate for that area during 1952. The rates for psychotic disorders increased from 1.7 to 2.4 per 1,000 in 1952. This was evident in all areas, continental, noncontinental, and shipboard. The over-all rate of character and behavior disorders rose to 8.4 from 6.6 per 1,000 in 1951. This was mainly the result of the sharp increase in continental activities. A moderate decline, however, was noted in noncontinental areas.

*Bacillary Dysentery.*—The incidence for this condition in fiscal year 1952 was 1.2 per 1,000, double the rate of the previous year. Outbreaks were more numerous, being reported in 7 out of the 12 months. In July, August, and September, practically all of the dysentery in the Navy was reported from ships. In October and November, outbreaks of bacillary dysentery were reported from Camp Lejeune, N. C. The last outbreak during the fiscal year was reported during May and June, 1952, and occurred on board the USS Newport News.

*Mortality.*—There were about 1,850 deaths due to nonbattle conditions, resulting in a provisional death rate of 1.8 per 1,000 average strength. This compares favorably with the rate for 1949, the year in which the death rate was the lowest in naval history. An improvement over the previous year was achieved despite the sinking of the U.S.S. Hobson with a loss of 176 men and the explosion aboard the U.S.S. St. Paul, which took 22 lives. Preliminary data indicate that motor vehicles were responsible for about 600 noncombat deaths and aviation accidents for about 400.

In the Navy and Marine Corps, there were 711 combat fatalities during fiscal year 1952. The combat death rate decreased from 3.1 per 1,000 in fiscal year 1951 to 0.7 per 1,000 in 1952. Truce negotiations accounted for a lull in battle activity and a decline in combat casualties.

The average number of patients on the sick list during 1952 in all naval medical facilities was just over 23,000, or 2,000 more than in the previous year. The peak load of patients was reached in February with a census of 25,113.

**International Society for Geographical Pathology.**—Dr. Howard T. Karsner, research advisor to the Surgeon General, U. S. Navy, was recently elected president of the American National Committee of the International Society for Geographic Pathology. This society was established in 1931 under the stimulus of Prof. M. Askanazy of Switzerland, while R. Roessle of Berlin, J. de Josselin de Jong of Holland, L. Aschoff of Germany, M. Roussy of France, M. J. Stewart of England, R. Henschen of Sweden, V. Moon of the United States, and many other pathologists took part in its organization. Its purpose is to bring together at one meeting the manifestations of a particular disease, common in various parts of the world, to compare them, and to arrive at conclusions concerning their cause and nature. Meetings are held at irregular intervals. A meeting devoted to cirrhosis of the liver was held in 1931 at Geneva, Switzerland; one concerning arteriosclerosis was held in 1934 at Utrecht, Holland; and another in 1937 at Stockholm, Sweden, was concerned with anemia. Not until 1952 was another meeting held, this one at Liége, Belgium, on the subject of hepatitis. In many countries there is a national committee that helps in the organization of programs. Dr. Karsner will assist the president of the international society in general arrangements and program agenda. Robert A. Moore, M.D., professor of pathology and dean, Faculty of Medicine, Washington University, St. Louis, Mo., is the president of the society. As president of the American National Committee of the society, Dr. Karsner will preside at the Fifth International Conference, which is to be held in Washington, D. C., in September, 1954.

**Personal.**—Capt. Otto L. Burton, MC, has been assigned director, Preventive Medicine Division, Bureau of Medicine and Surgery. His previous assignment was force medical officer on the staff, Commander Service Force, Pacific Fleet. Capt. Robert W. Babione, MC, the present director, Preventive Medicine Division, was detached on Dec. 20, 1952, to report to the Commander Fleet Activities, Sasebo, Japan.

# FOREIGN LETTERS

## BRAZIL

**Psychic Troubles in Cranioencephalic Trauma of Children.**—Dr. Orlando S. Duarte, psychiatrist of the Rio de Janeiro Getulio Vargas Hospital, reported recently on the treatment of 120 children, from 1 to 12 years old, suffering from cranioencephalic trauma. The duration of the illness ranged from 2 to 42 days (average 7.1 days), with six deaths (5.0%). The commonest psychic trouble was somnolence, observed in 32 cases (26.7%), out of which in 26 there was no fracture of the cranial bones. This symptom probably corresponds to a simple cerebral dysfunction without lesion of the neuronic structures. Coma was next (19 cases, or 15.8%) with a high fatality rate (31.5%). In patients who were operated on or autopsied by the author, he found cortical or subcortical diffuse contusion with the exception of cases in which there was compression by a fluid. Loss of consciousness was observed in 16 cases (13.3%), all characterized by an apparent absence of severity but demonstrating a greater degree of impairment. It results from a complete paralysis of cerebral functions appearing soon after the accident. Amnesia, present in 13 cases (10.8%), was of a mixed character, retrograde and post-traumatic, always with predominance of one or the other type. It continued for a variable period of time, ranging from a few minutes to 13 days. Long periods of amnesia were present in very few cases with more serious structural damage. They were very similar to those observed in war shock. Restlessness, also observed in 13 cases (10.8%), seemed to be caused by the liberation of the lower centers. Obnubilation, present in 13 cases (10.8%), was discovered only after careful examination, being very similar to petit mal. Fear, present in two cases (1.6%), was connected with a depressive state. It was not a neurotic manifestation but rather, believes the author, a characteristic development of the trauma. It was commoner as a late than an immediate psychic phenomenon. Mental confusion, psychogenic reaction, and post-traumatic mental impairment were observed in one case each (0.8%). Mental confusion was observed in a case presenting an acute mental insufficiency, total and diffuse, transient and regressive, with obnubilation, loss of understanding, and loss of orientation. It was not similar to traumatic delirium in which there is a psychotic character. The case showing psychogenic reaction was of the autist type, leading the author to think of it as an equivalent of child hostility commonly observed in children reared under too strict discipline, and similar to troubles frequently described after poliomyelitis. These troubles sometimes leave a sequel in the mental life of the patient. The case presenting a post-traumatic impairment showed a mixture of psychic and neurological tendencies (extrapyramidal) resembling those related to arteriosclerotic dementia. When the child left the hospital, 13 days after the accident, there were still evidences of amnesia and a marked emotional irritability.

**Surgical Treatment of Bronchiectasis.**—Contrary to occurrences in other countries, bronchiectasis is a disease rarely referred to in Brazilian medical literature or even observed in hospitals. Patients live many years with what is thought to be chronic bronchitis attributed to an excess of smoking, until severe complications occur that lead to more careful examination and a late correct diagnosis. Recently, Drs. Euryclides J. Zerbini and Edgard S. de San Juan, of the department of clinical surgery, São Paulo State University, reported on the surgical treatment of 23 patients having bronchiectasis operated on by them. Eight patients were between 31 and 40 years of age (34.8%), and the majority of patients were males (78.0%). More than half of the patients showed symptoms for five years or more. In many patients the symptoms of bronchiectasis appeared after sinusitis (5 patients, or 21.7%, had had a frontal or maxillary sinus infection) or after pneumonia (14 patients, or 60.9%). Of the 23 patients, 2 showed bronchiectasis directly related to the aspiration of a foreign body. Coughing and expectoration were found in all patients, but the thoracic pain corresponding to the localization of the bronchial process appeared in only 14 (60.9%). Five patients had hemoptysis (21.7%), the quantity of blood lost varying from 50 to 2,000 cc. Sixteen patients (69.6%) showed marked loss of weight and signs of intoxication. Hippocratic fingers were observed in five (21.7%). Roentgenograms disclosed suggestive signs of bronchiectasis such as visible bronchial design and atelectasis, the latter having been found in eight patients (34.7%). The bronchogram is indispensable to a correct diagnosis and to a careful study of the localization and the morphological changes of the bronchi. The bronchoscopy must always be done, as in many cases the etiology of bronchiectasis is easily discovered by it (foreign bodies, adenomas, and cancer). In highly infected patients, the bronchial aspiration prepares them for pulmonary resection; furthermore, it is by the endoscopy that the side to be treated first in bilateral cases is selected. Of the 23 cases studied, 9 were bilateral (39.1%) and 14 unilateral (60.9%). The more frequently infected parts of the lungs were, in decreasing order: the right inferior lobe 17 cases, or 73.9%; the left inferior lobe 14 cases, or 60.9%; the medial right lobe 7 cases, or 30.4%; the lingula 6 cases, or 26.1%; and finally the left superior and the right superior lobes 2 cases each, or 8.7%. Among 14 cases of lesions of the left inferior lobe there were also concomitant lesion of the lingula in 6 cases (26.1%). The more frequent complications of bronchiectasis were lung abscess (five cases, or 21.8%), pleural empyema, cerebral abscess, and amyloidosis (one case each, or 4.3%).

Of the 23 patients, 6 had medical treatment and the other 17 were treated by total or partial resection of the diseased tissue. On the 17 patients submitted to surgical treatment, 22 operations were performed; 1 patient was operated on three times: the first time for the resection of the left inferior lobe and the lingula, the second time for the right inferior lobe, and the third time for the medial lobe. There were no fatalities in the cases submitted to pulmonary resection. As postoperative complications, the authors note a case of pleural empyema and one of organized hemothorax. They emphasize that in the treatment of bronchiectasis the cure is effected only by the resection of the diseased pulmonary tissue. The 11 patients submitted to a resection of all bronchiectatic lesions are now cured. In six patients the major portion of the bronchiectatic lung was resected, but still there persisted zones with lesions; two of these patients are without symptoms, two are improved, and two are unchanged. The patients submitted to medical treatment (six cases) showed marked improvement in 50% of the cases; the remaining did not benefit by the treatment.

## DENMARK

**Reform of the M.D. Degree.**—The degree of doctor of medicine at the two Danish universities, Aarhus and Copenhagen, is a much-coveted distinction about which there have been many complaints in the past. The candidate for this degree has had to present a monograph including not only his own work but also the literature on the subject, with a discussion and conclusion, all incorporated in a bulky volume of some 150 to 300 printed pages. If the author has confined himself to the Danish language, having found the cost of translation into some other language prohibitive, his work has been foredoomed to oblivion for want of readers familiar with Danish. Other objections to the old system are that the publication of such a big book takes a long time and is very costly. Candidates for this degree have often been tempted to choose a subject for research with a comparatively limited scope instead of launching out into more ambitious and, perhaps, more important research.

In the light of these and other criticisms, the medical faculties of Aarhus and Copenhagen have now worked out new rules for their respective M.D. degrees. In the future, a candidate for this

The items in these letters are contributed by regular correspondents in the various foreign countries.

degree may hope to gain it either in the old way or in a new way, the essence of which is that he may achieve his aim by presenting earlier publications reflecting original work. These earlier publications must be supplemented by a general survey covering the problems already dealt with in his earlier, published works. Such a survey should seldom cover more than 40 to 50 printed pages. The changes should not be interpreted as an attempt to relax the high standard of the M.D. degree but rather to bring it more into line with the requirements of the present time. This degree confers *jus docendi*, the legal right to teach and not merely to practice medicine. Clarity of reasoning, of language, and of presentation of arguments are therefore required of candidates for this degree, and they must show these qualities in their general survey of their subject.

**Prefrontal Lobotomy for Criminals.**—At the Psychopathic Institute in Herstedvester (an organization directed by Dr. Georg K. Stürup), much attention has lately been paid to prefrontal lobotomy as a solution for the problems raised by certain criminal psychopaths for whom other less radical measures have proved futile. In a communication on the subject to *Nordisk Medicin* for Sept. 12, 1952, Dr. Ebbe J. Linnemann points out that hitherto little has been published concerning lobotomy as a corrective measure for criminal tendencies in psychopaths. Indeed, so little is known of this particular problem that it is still debatable whether this operation promotes or counteracts criminal tendencies. To be sure, no psychopath who has undergone lobotomy has hitherto been convicted of murder or any other major crime, but it is a far cry from such offenses to the minor delinquencies that may conceivably be indulged in by psychopaths after lobotomy has suppressed certain inhibitions.

Dr. Linnemann's contribution to this discussion consists of detailed records of three women and three men who underwent bilateral prefrontal lobotomy as the ultimate solution after more conventional medical and psychiatric treatment had proved futile. Broadly speaking, the results justified the means, with a diminution of criminal and certain other morbid tendencies, offering a prospect at any rate of partial recovery. But in one case, that of a woman who had incessantly wandered in and out of asylums and psychiatric hospitals for many years, her first conviction was for a series of minor pilferings, all of which she had indulged in after the operation. Yet it is probable that she had also pilfered before the operation, although there had been no formal conviction on record. The influence of the operation on the sexual life of the patients was by no means uniform. While in one case it had been followed by frigidity, it had done little to change the sex instincts and habits in another case. In every case, the affective reactions were considerably subdued after the operation, and one man and one woman were socially rehabilitated without manifestations of criminality for several years. In three other cases the outlook was favorable, but Dr. Linnemann is cautious with regard to the ultimate prognosis, since the observation period was still short.

**Incidence of Peptic Ulcer in Denmark.**—In October, 1940, and again in October, 1948, a nationwide census of peptic ulcers was undertaken under the auspices of the Danish National Health Service. The questionnaire, addressed to every medical practitioner, required detailed information concerning the cases of peptic ulcer diagnosed or treated during these two months, space being provided for the recording of such information as the location of the ulcer, radiological examinations, operations, manifest hemorrhages, and fatalities. In 1940, 84.6% of the physicians answered this questionnaire, the corresponding figure for 1948 being 83.2%.

A statistical analysis of this material has been undertaken by Dr. Gunnar Alsted, whose report in *Ugeskrift for Laeger* for Sept. 11, 1952, brings out some curious and challenging observations. The number of reported cases of peptic ulcer rose from 4,159 in 1940 (3,113 males and 1,046 females) to 6,854 (5,444 males and 1,410 females) in 1948. It will thus be seen that the ratio of 3 males to 1 female in 1940 changed to 4 males to 1 female in 1948, and while the incidence of peptic ulcer was almost doubled for males during the period under review, there was only a slight rise for females. For both sexes together there was a rise in the same period from 11 to 16.9 per 10,000 inhabitants.

In Dr. Alsted's opinion, the almost complete disappearance of ulcer of the corpus of the stomach in young women during the first decades of this century may well have been due to the discarding of their corsets. By the same token he correlates the trebling of the incidence of ulcer of the corpus in Danish males, aged 40 to 50, between 1940 and 1948, with the discarding of braces and the wearing of belts. As for the increased frequency of duodenal ulcer in both sexes between 1940 and 1948, Dr. Alsted is inclined to trace it in part to heavy cigarette smoking. The comparative immunity to peptic ulcer enjoyed in the past by male workers on the land may reflect their comparative freedom from mental strain, but the growing mechanization of farm work during the past 10 to 15 years may perhaps account for the rising peptic ulcer rate in workers whose adoption of machine methods in farming has imposed a growing mental strain on them.

## ISRAEL

**Shigella and Salmonella Research.**—W. Silberstein and C. B. Gerichter, of the government central laboratories in Jerusalem, report their results of investigations concerning the appearance of Salmonella bacteria in Israel. In 1949 the National Salmonella Centre for the State of Israel was established by the Ministry of Health at the government central laboratories in Jerusalem. In the course of two and a half years 319 strains of 31 serologic types were sent in, all of them except one originating from a human source. (Salmonella typhosa was not included in this survey, 200 strains of which were investigated in the same period.) There is no doubt that this relatively small number of strains sent for identification does not represent all of the Salmonella strains to be found in the country during that period. Nevertheless, conclusions may be drawn in regard to the geographical distribution of the different types, since they were sent from various parts of the country.

The majority of the three types S. paratyphi A, S. paratyphi B, and S. paratyphi C were isolated from patients showing clear symptoms of enteric fever, S. paratyphi C appearing in a smaller number of cases than the two others, a fact well known in Israel; however, there has been a constant increase of S. paratyphi C in comparison with previous years. In some cases strains of these three types were found in healthy carriers. Importance is to be attached to the fact that strains of these three types and others have been found in persons handling foodstuffs. Such findings were made possible by the issuance of orders by the authorities for the examination of stools of persons dealing with such materials. Besides the three types mentioned, strains of S. Kottbus, S. anatis, and S. Meleagris were also found on food dealers.

The most frequent types in Israel are: S. paratyphi A, S. paratyphi B, S. typhimurium, S. Newport, and lately also S. Meleagris. Strains of S. enteritidis are encountered in relatively small numbers. In the past few years types hitherto unknown in this country made their appearance, e. g., S. Stanley, S. Oslo, S. Braenderup, S. Concord, S. Potsdam, S. Dublin, S. Panama, S. Meleagris, S. Taksony, S. Havana, S. Worthington, S. Sundsvall, and S. Gaminara. Furthermore, five new strains were isolated: S. Haifa, S. Jerusalem, S. Ness-ziona, S. Emek, and S. Tel-hasomer. It must be assumed that at least some of these types appeared in Israel as a result of the mass immigration of the past few years. It is quite possible that the source of some types were foodstuffs imported from abroad, i. e., egg powder. The serologic Salmonella types published hitherto in Israel amounts to a total of 44.

Raja Sapiro, Haifa, from the Central Laboratory of the Kupath Cholim, has isolated and identified a new Shigella bacteria in 27 cases of clinical dysentery. It has no serologic relationship to any of the dysentery bacilli so far described. W. H. Ewing, United States International Shigella Center, and S. Szturm-Rubinstein, Pasteur Institute, Paris, found this strain to be identical with a new Shigella described by Szturm, Piéchaud, and Néel, in 1950, and by Ewing and Taylor, in 1951, which had been named by Ewing provisional Shigella boydii lo. In all 27 cases, the colonies produced with this strain in primary cultures were numerous, the exudate typical for bacillary dysentery, and the clinical picture moderately severe.

## LONDON

**Insulin Not a Monopoly.**—In December, 1950, the Board of Trade, acting under the terms of the Monopolies and Restrictive Practices (Inquiry and Control) Act, 1948, requested the Monopolies and Restrictive Practices Commission to investigate the question of whether the supply of insulin in this country constituted a monopoly under the terms of the act. The commission's report, which has now been published, is a complete exoneration of the manufacturers from any such accusation; the commissioners "find that the arrangements now made by the British Insulin Manufacturers, individually and collectively, for the supply of insulin operate and may be expected to operate in the public interest and we do not recommend that any of them should be discontinued."

All of the insulin now supplied in the United Kingdom is produced by four companies. Since February, 1941, these companies have been loosely organized into the British Insulin Manufacturers (B.I.M.). Prices and discounts for British-made insulin are uniform. In 1950 the total insulin sales by these manufacturers amounted to a quantity of 3,131,900,000 units and a value of £1,266,722, of which 55.8% (by quantity) and 60.7% (by value) was supplied to the home market. Eighty per cent of the insulin consumed in this country is distributed by retail chemists and the remainder by hospitals, with the exception of a very small amount (in 1950 less than ⅓%) obtained by the Ministry of Health for service requirements. By law, the only traders who may sell insulin at retail in this country are registered pharmacists. It is estimated that there are 200,000 diabetics in the United Kingdom, of whom 60 to 70% are receiving insulin. The great majority of these obtain their supplies through the National Health Service. A labor force of approximately 250 is employed in manufacturing insulin in the United Kingdom, excluding the force required for the sterility and biological tests. A relatively high proportion of the personnel possesses professional or technical qualifications.

The discovery of insulin at the University of Toronto in the summer of 1922 was followed immediately by the decision to apply for patents in Canada, the United States, and Great Britain. The patents were assigned to the governors of the University of Toronto "to prevent the exploitation of the public and to secure some control over the quality of the commercial product." The first British patent was granted on June 13, 1922. Prior to this the University of Toronto suggested to the Medical Research Council in Great Britain that its prospective rights under the patent should be assigned to the council. The Medical Research Council ("though averse in principle to any proposal for the patenting of medical preparations") accepted the university's offer and decided to control insulin production by licensing under the British patent on the condition, which was accepted by the university, that "the assignment should be free, no royalties being paid to the University from this country for the use of the patent." In September, 1922, two of the Medical Research Council's officers, Dr. (now Sir Henry) Dale and Dr. W. H. Dudley visited Toronto to discuss with Dr. Best and Dr. Banting the problems involved in the commercial production of insulin. British-made insulin was first marketed in April, 1923.

During the period from 1923 to 1927, the great bulk of the British requirements of ox pancreas was obtained from slaughterhouses in Great Britain. In 1923 the Medical Research Council took out a patent for a process of purification. English manufacturers were given permission to use the process freely, and the patent rights were extended, at the request of the University of Toronto, to Canada and the United States. The council's rights in these countries were assigned to the University of Toronto for exercise by the latter. During 1924, insulin production in Great Britain increased sufficiently to meet home demands and to allow some exports. The University of Toronto, which held the patent rights in certain overseas countries, issued to each of the English manufacturers a license to allow them to distribute insulin to these countries, other than Canada and the United States, imposing a royalty payment of 5% on such exports. These royalty payments have now ceased to be made. British-packed insulin has never been sold in Canada or the United States. During this period, although there was no control over imports of insulin into Britain, such imports were in relatively small quantities. During the period 1928 to 1940, a certain amount of German and Danish insulin was imported. In March, 1932, insulin became subject to the general ad valorem duty chargeable under the Import Duties Act, 1932. In December, 1933, insulin and its salts were added to the list of fine chemicals, which, under the Safeguarding of Industries Act, 1921, were subject to 33⅓% key industry duty. At the same time, the British insulin manufacturers undertook not to raise their prices; actually they were lowered. In the Finance Act, 1934, imported insulin was entirely freed from duty. Throughout this period collaboration continued between the insulin manufacturers. There was also an increasing use of imported pancreas, and home collection practically stopped between 1934 and 1939.

In February, 1941, the first meeting of the B.I.M. was held to discuss "the threat to pancreas supplies, the possibility of loss of insulin stocks or damage to plants from enemy action, and a considerable and understandable degree of apprehension on the part of the medical profession, the pharmaceutical trade and the diabetic public, which had resulted in some 'panic' buying of insulin and an artificial scarcity." One of the first steps taken was to make successful representation to the Ministry of Supply for the obtaining of considerable quantities of solid insulin from the United States under lend-lease in 1941 and 1942, to build up a reserve stock. There was increased collaboration at all levels, one of the most important results of which was a remarkable increase in the insulin yield per pound of pancreas. At the same time an educational campaign was undertaken, in cooperation with the Ministry of Food, among workers in slaughterhouses in this country, explaining the need for careful removal, trimming, and quick freezing of pancreas. This led to an increased yield of insulin from home-produced pancreas. In January, 1944, largely as a result of suggestions made by the Diabetic Association, a uniform scheme for labels and cartons that would clearly differentiate between the different kinds and strengths of insulin was introduced by all manufacturers of insulin. In the postwar years negotiations were carried out for increased collaboration between the B.I.M., American manufacturers of insulin, and the University of Toronto, which manufactures insulin commercially in its associated Connaught Laboratories and controls the manufacture of packed insulin in the United States through patent licenses. These negotiations produced little in the way of practical results.

The greater part of ox pancreas, the principal source of insulin in this country, is still imported. The price for British ox pancreas in 1950 was considerably less than the average price of imported glands, but the yield of insulin from British glands is poorer than that from imported glands. New sources of supply are constantly being investigated in order to ensure that glands shall be available at the lowest practicable price. The present method of insulin manufacture as used by each of the British manufacturers is essentially the same. The process is not protected by patents but is secret. As far as price is concerned, the members of the B.I.M. charge common prices. There is a general unwritten understanding that no company shall alter its prices without first informing the others and discussing the proposed changes with them, but any manufacturer is free to sell at the lowest price he desires. On the other hand, it is pointed out by the B.I.M. that "it is an inevitable concomitant of the free exchange of information in the technical field that the manufacturers engaged in technical collaboration will not exploit unfairly the advantages so obtained." The success that British manufacturers have achieved in supplying insulin at the lowest possible cost is strikingly revealed in a table in the report showing the retail prices of 5 cc. (20 units per cubic centimeter) packs of unmodified insulin from 1923 to this year. In April, 1923, this price was 25s., and in July, 1952, it was 1s. 5½d. Actually the lowest price achieved was 1s. in 1944. The subsequent increase is almost entirely due to the increased cost of pancreas; the 1950 average price of pancreas (home and imported) was about four times that of the 1939 price. The importance of this increased cost of pancreas is evident when it is realized that the cost of pancreas represents approximately 45% of factory cost. It is pointed out in the report that insulin prices in the United Kingdom are the lowest in the world, with the possible exception of those charged in Scandinavia.

Finally, it is of interest to note some of the views concerning British insulin and its manufacture, which the Commission obtained from independent authorities. "The Ministry of Health has told us that in its view and that of the National Institute of Medical Research, the quality of British insulin is unsurpassed. It considers the members of the B.I.M. to be extremely public-spirited in all that concerns the interest of diabetics. . . . The Director of the Department of Biological Standards of the National Institute for Medical Research has said that he has a high opinion of the B.I.M.'s work, both in research and in other fields connected with insulin production." The physician-in-charge of the Diabetic Clinic at King's College Hospital, London, who is also chairman of the Diabetic Association, has told the commission that the quality of British insulin is first class, that he has the highest respect for members of the B.I.M., and that, in his view, the United Kingdom market is adequately supplied and the importation of additional brands would only cause confusion. The 16 selected hospitals with diabetic clinics that were also consulted by the commission expressed satisfaction with the present insulin situation.

## MEXICO

**Studies on Malnutrition.**—Since 1946, the Children's Hospital (Mexico City) has been studying, through a special service of Studies in Malnutrition, the problem of malnutrition in Mexican children. In the June issue of its Medical Bulletin, Drs. Gómez, Ramos Galván, Cravioto, and Frenk summarize their findings and compare them to those of Brock and Autret and the data published in the *Chronicle of the World Health Organization* (6:61, 1952) about kwashiorkor, an African disease of children, which the Mexican investigators consider the equivalent of the severe states of malnutrition found in Mexico.

According to the aforementioned paper, the malnutrition of children in Mexico, when severe (the authors qualify it as third degree), shows the following characteristics:

(1) delay in growth and physical development; (2) changes in skin pigmentation and hair color; (3) edema, especially in lower extremities, hands, and face, in which the areas are soft, cold, and not painful; (4) fatty infiltration or degeneration of the liver, or both; (5) hypoproteinemia with hypoalbuminemia, low alpha globulins, and high gamma globulins; (6) anorexia, intense and refractory; (7) anemia, seldom severe; (8) marked diminution of the enzymatic activity of the duodenal contents; (9) dystrophic changes in skin; (10) mental indifference and irritability; and (11) a high mortality when treatment is not instituted opportunely. This picture is entirely similar to that described by Brock and Autret in African children, except in three respects: 1. The color of the hair in African children becomes red, and in the Mexican it turns yellowish. 2. Macroscopic steatorrhea, reported as frequent in Africa, is rare in Mexico. 3. The so-called pot-belly appears in Mexico only in the stages of recuperation. Another similarity between the malnutrition observed in Mexican children and kwashiorkor is the etiology, which in both seems to be the almost absolute absence of animal proteins in the diet.

Usually, prognosis is very poor and complications of infectious nature (such as bronchopneumonia) is a frequent cause of the fatal termination. Treatment, as recommended by the Mexican investigators, consists in rehydration; transfusions of whole blood, plasma, or hydrolized proteins; restoration of electrolytes; and forced feeding of acidified skimmed milk in the severest cases. When the evolution is satisfactory, the basis of subsequent treatment is the diet, which must be high in proteins.

**Etiology of Laënnec's Cirrhosis.**—The high incidence of Laënnec's cirrhosis in Mexico is well known. In order to study the role of some etiopathological factors in the production of cirrhosis, Sepúlveda, Rojas, and Landa reviewed the first 150 cases of the Hospital de Enfermedades de la Nutrición, in whom the clinical diagnosis was verified by histological means (autopsy or liver biopsy). In every case a history of alcoholism and/or malnutrition were carefully looked for. Syphilis, tuberculosis, brucellosis, and malaria were also systematically investigated. The following tests and studies were done routinely: (1) liver function tests (direct and indirect bilirubin determinations, bromosulphthalein retention, blood proteins and their components, total and esterified cholesterol, prothrombin time, cephalin cholesterol flocculation, and thymol turbidity and flocculation); (2) blood cell counts; urinalysis; investigation of parasites in feces; serological reactions for syphilis; and (3) radiological examination of thorax.

Three control groups were established: one of patients with a history of malnutrition and alcoholism; another of alcoholic patients with a history of an adequate diet; and a last one of relatives of cirrhotic patients, i. e., persons who had the same type of diet as the patients with cirrhosis.

The information gathered in this study agrees with the hypothesis that malnutrition by itself is quite capable of causing liver damage; alcoholism alone also may produce hepatic lesions, although this occurs less frequently. According to the observations of Sepúlveda and his associates, it is the combination of both factors, malnutrition and alcoholism, that produces liver damage in a higher proportion of cases (81.3%) than malnutrition or alcoholism acting separately (7.3 and 6.6% respectively).

Because of these facts and of the finding that the roles of syphilis, tuberculosis, brucellosis, and malaria could not be considered of importance, the authors conclude, in a paper published in the *Revista de Investigación Clínica* (October, 1952), that malnutrition and alcoholism acting together are by far the most important factor in the etiology of Laënnec's cirrhosis in Mexico.

**Damon Runyon Fund Grant to Hospital.**—In 1951, the Damon Runyon Fund for Cancer Research granted the sum of $5,000 to the Hospital de Enfermedades de la Nutrición (Mexico City) for the study of uterine cancer. Since then, a team of endocrinology and cancer specialists have been investigating the effect of steroids on the evolution of carcinoma of the corpus uteri and cervix. The possibility that some of these substances have an anticarcinogenetic effect has been investigated, through their use in patients with uterine cancer (grades 3 and 4, League of Nations scale); during the treatment the course of the lesions is followed fortnightly by means of cytological and histopathological studies and by the patterns of excretion of hormones in the urine. This investigation will continue this year and it has recently been announced that the Damon Runyon Fund has again allocated $5,000 for this purpose.

## PARIS

**Gastric or Duodenal Aspiration.**—In a recent discussion at the National Academy of Surgery on the treatment of ulcers and abdominal penetrating wounds by gastric or duodenal aspiration, G. Kropff and M. Quénu reported their results in 17 patients showing signs of perforation and treated with success by gastric aspiration. The only complication, a subphrenic abscess, healed without intervention. In 13 patients the diagnosis of perforation was certain, and it was plausible in 3. Seillé stated that failures are possible; often improvement is followed by an exacerbation. Professor Sénèque insists that this method necessitates an unequivocal diagnosis, which is difficult to establish. Gueulette reported several cases in which he found, in the course of operation, an impervious obturation of the perforation through a thick exudate. In such cases he closed the abdomen without suturing the ulcer. According to Professor Quénu, the most serious problem arises from an error in diagnosis. He found two cases of acute appendicitis, the consequences of which are not alarming, he believes, if the patient is properly watched. Risks of error are diminished by a careful clinical examination and abdominal radiography. According to him, a patient with liquid in the abdomen, an excited patient who tears away his drain, or one who is bleeding at the time of his perforation must be operated on. Delorme and Sauvage reported a new indication for duodenal aspiration. Eight wounded patients with penetrating wounds in the abdomen, confirmed by radiography, were all cured by gastroduodenal aspiration. The authors called attention to the analogy existing between these wounds and perforations of ulcers; they believe that this new method of treating abdominal penetrating wounds is specially indicated in cases in which no surgeon is available or while awaiting his arrival.

# CORRESPONDENCE

## ADMIRAL PUGH REPLIES TO EDITORIAL

*To the Editor:*—Thanks for sending me the tear sheet from THE JOURNAL bearing on my recent statements before the Association of Military Surgeons here in Washington. As is inevitable when an author is quoted out of context, or when only fragments of a general statement are used by the press, almost any kind of impression may be conveyed. If my paper had been heard or read in its entirety, I think there is little likelihood of the reader's or hearer's having been so erroneously impressed.

While there are few points encompassed in my paper that have not already been elaborated on in response to the individual letters I have received, I would, in the interest of reassuring those for whom I meant no criticism, like to reiterate certain facts I have already proffered to the President of the American Medical Association and to the Secretary and General Manager of the American Dental Association.

First, let me say that, although my paper was screened by the agents not only of the Navy Department but of the National Defense Department as well, whose mission it is to pass on such releases, I and I alone assume the responsibility for every utterance or for every expression, or implication thereof, contained in the paper in point. That there were some who misinterpreted my meaning, and therefore were disposed to try to wear a shoe that was never intended for them, is genuinely regretted.

Unless my paper is published in its entirety by THE JOURNAL, I think it would be difficult to dissuade those wrongly impressed from their preformed opinions. The reader, I think, would definitely recognize from the tenor and contents of paragraph 5 of my paper that specific reference was being made to an element or segment of the professions of medicine and dentistry and certainly not to the professions as a whole. Reference was definitively made to that segment, many of whom have never been in the service, although reckoned as being obligated to serve, and who continue to advance as their reason for their unwillingness to serve a lack of attractiveness on the part of the service.

Reference to the record will reveal the list of measures that have been implemented in an effort to better the lot of the service doctor since World War II to be a long and impressive one. It is after contemplation of such a list that I have been constrained to express wonderment as to how much further the services can be expected to go.

Inasmuch as the press has shown a disposition to play on certain terms used by me in the paper, I would offer brief comment in extenuation. First, with respect to the word avarice, I used it in the sense that it connotes an inordinate desire for material gain, and I would submit here that my conclusion as to this inordinate desire's constituting a principal determining element of attractiveness is inescapable. I base this conviction on the testimony of a host of doctors, to which I have been exposed for the past several years.

Reference is also made to my having employed the word greed (see line 3, paragraph 3 of THE JOURNAL statement under date of Nov. 29, page 1312). That is a misstatement; the word greed will not be found in my paper. To come next to the word pantywaist, that word was used in a question and with a distinct connotation of incredulity. The implication, I think, was clear that it was incredible to me that the disciples of the profession of medicine by and large, if weighed in the balance, would be found wanting in intestinal fortitude. Another word that has come in for its share of bandying about is prima donna. I did not use that word as a qualifying term for a doctor merely because he had expressed an interest in obtaining further postgraduate education, as a few of my critics would have it appear. I would have it apply only to some (I would not say a large number of doctors) but definitely some whose interest in that respect overshadows the attribute of patriotism, a quality with which American doctors of the past have demonstrated themselves to have been richly endowed.

I take no exception to most physicians, like most civilians, preferring a nonmilitary life. That is as it should be, but I would point out that precisely that sentiment obtains with respect to practically all of those presently engaged in mortal conflict in Korea and many this side of Korea. I am aware too of what the Office of Business Economics of the Department of Commerce reports reveal with respect to income figures for physicians, hence my qualification in the last line on page 5 of my paper in which the word fanciful is used.

Relative to the matter of waste, I think there are few who have been engaged in war who will not regard the whole ordeal as waste, but I fail to see how their concern over wastefulness could constitute much of a deterrent with the group of doctors and dentists at whom my criticism was leveled, since they are not war veterans. It in fact was, and will continue to be, my genuine concern for the interests of those many doctors who have earned the right not to be further disturbed in their present pursuits, or to be released to civilian life as expeditiously as possible, that prompted my criticism of the group in point. It was my thought that the multitude of doctors whose welfare I sought to protect would appreciate my aim.

As the incumbent of my office it behooves me to be concerned about an adequate supply of medical officers to meet the needs primarily of the Navy and Marine Corps. It is my concern not only to keep sufficient doctors at the front in Korea to assure the best quality and measure of professional coverage possible but to provide for the relief of those doctors so serving as promptly as they have every right to expect it. This desire and aim have been difficult of accomplishment. We have obtained an adequate number of excellent doctors, to be sure, but only under the stimulus of the draft law and by reliance on our faithful reserves. The draft law must be distasteful to all of us alike, whether in or out of uniform, and I am sure we all devoutly wish that some means could be discovered to obviate the necessity for its reenactment. Nothing so far introduced, including soft words and entreaties, offers much hope. The practice of calling and recalling reserves in the Navy to the end that those more immediately and positively obligated may remain out of uniform, poses a devastating morale factor within the ranks of the service's most patient and deserving element—its wonderful reserve component. I would enjoin service-eligible doctors only to share with their contemporaries and confrères the responsibility of meeting the requirement the armed services must rely upon them to meet.

Unless and until the services are forced to ask the Congress of the United States to provide an independent means of obtaining medical manpower essential to meeting their needs, there is no place to turn but to civilian medicine. That is what I have done, and, while I have not been disposed to mince words in my remarks relative to a certain segment, I do not consider that I have cast any slur on the profession as a whole nor any element thereof. As a matter of fact, the segment to which my pointed reference pertained comprises members far junior in years to me, and my attitude toward their number was, and is, very much in the nature of a father's attitude toward his sons.

Why any representative of the American Medical Association or the American Dental Association should have felt disposed to consider my comments as constituting an affront to their organizations or to their professions is better known to them than to me. It does, nevertheless, seem somewhat incongruous for these organizations to so vehemently rally to the defense of the same segments of their respective groups whose members have in recent years responded in so cavalier a manner to the importunities of their leaders in the selfsame cause as the one I now espouse. Witness the response to the combined efforts of the A. M. A. and the so-called moral suasion recruitment campaigns in 1949.

I regret that so much comment should have appeared in the public press that was obviously prompted more by heat than light. I have, for 35 years, held the profession of medicine and

the American Medical Association in high esteem and have striven, as a member of that profession and that organization, to be a credit to both. My genuine appreciation of the support and assistance rendered by the American Medical Association and the American Dental Association, as organizations or on the part of their various members, in behalf of service medicine, has been voiced by me time and again, and it is definitely my intention, as long as I wear the uniform of the United States Navy, to continue to lean on and to expect from organized civilian medicine and dentistry their wholehearted assistance and support.

REAR ADM. LAMONT PUGH (MC) USN
Surgeon General of the Navy
Washington, D. C.

## CONFUSION BETWEEN PHENYLBUTAZONE AND BUTAPYRIN®

*To the Editor:*—Recent reports in THE JOURNAL and elsewhere have described the clinical use of a new anti-arthritic agent, phenylbutazone (butazolidin®) and a related preparation, butapyrin® (irgapyrin®). The association of the two products in the same reports has led to some confusion, which it is the purpose of this letter to dispel.

Phenylbutazone, presently issued under the trade name of butazolidin,® is a new synthetic compound, which is chemically 3,5-dioxo-1,2-diphenyl-4-n-butyl pyrazolidine. It is commercially available on prescription in the form of 100 and 200 mg. tablets for oral administration. Investigators have described the experimental use of solutions of the drug by intramuscular administration, but presently the product is not commercially available in ampul form.

Butapyrin,® known outside the United States as irgapyrin,® is a combination product consisting of phenylbutazone and aminopyrine in equal parts. We wish to emphasize that butapyrin® never has been, and still is not, commercially available within the United States. For a limited period it was made available on an experimental basis to qualified investigators. All of these investigators have subsequently switched their studies to the investigation of phenylbutazone alone. The inclusion in their reports of results obtained with butapyrin® is obviously of practical significance only to the extent to which these results may have been attributable to the phenylbutazone component alone. From these remarks it will readily be seen that pharmacists are not in a position to fill prescriptions for any of the mentioned preparations except the tablets of butazolidin® (phenylbutazone) for oral administration.

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## PERORAL ENDOSCOPY

*To the Editor:*—I enjoyed the article "Preparation of Patients for Peroral Endoscopy" by Olsen and Pender, in the Nov. 1, 1952, issue of THE JOURNAL, page 842, but would like to point out that in bronchoscopy Holinger does not recommend the preoperative use of atropine because it inhibits the bronchial secretions, which should be avoided in asthmatics and in any patient with bronchopulmonary suppuration. The practice of applying topical anesthesia in the pyriform sinuses in bronchoscopy is also dispensed with by Holinger, because he feels that the "areas of gagging" in the procedure are confined to the root of the tongue and the posterior wall of the pharynx.

In esophagoscopy, besides the usual topical and preoperative medication (including atropine), Holinger instills 2 cc. of a 10% cocaine solution into the adult larynx to subdue the coughing that occurs during esophagoscopy. As for water soluble opaque solutions versus iodized oil (lipiodol®) in bronchography, the water soluble solutions are rarely used because of the pulmonary reaction as mentioned in the Olsen-Pender article and also because the pictures have to be completed within five minutes, since the solution disappears rapidly.

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## LOEFFLER'S SYNDROME

*To the Editor:*—I have just read with interest the article "Gastric Lesion of Loeffler's Syndrome" by Ruzic and others in the June 7, 1952, issue of THE JOURNAL, page 534. I have been engaged in studies on Loeffler's Syndrome for about 10 years. The disease is widely prevalent on the west coast of India. I have a record of about 1,000 cases or more, and my observations rather convincingly prove the view tentatively put forward by these authors that this syndrome can and does manifest itself in affections of any tissue of the body, from the superficial skin and scalp to the brain, heart, or pancreas.

In the article, the authors have established their finding by the thoroughness of their investigation of the one case detailed therein. Although the lack of advanced laboratory facilities in this part of the world has been a handicap to me, I believe the number and variety of the cases in my collection do make up for the deficiency in laboratory x-ray and biopsy studies. In one recent case, for example, a man of about 60 complaining of almost continuous abdominal pain and vomiting was examined elsewhere before coming to me. After fluoroscopy had been performed, he was advised to have an operation. Because of this advice, and because of his age, cancer of the stomach seemed a possibility, which had first to be ruled out, although examination of his blood clearly showed eosinophilia. He was therefore sent for radiological examination. Only a single photograph was taken. This negative did not suggest cancer, and the patient was accordingly treated for eosinophilia. All his symptoms subsided, and he has gained weight and is now free from any complaints.

The eosinophil count may vary from time to time and may even remain normal for long periods of time, though the patient may be showing all the symptoms of the disease. That means the blood cell count by itself should not be taken as an absolutely essential criterion for the diagnosis of this disease, especially when it is made only once or twice. I have also noted that the disease may in the same patient manifest itself successively in different systems of the body, a point that has not been sufficiently emphasized by the above-mentioned authors, although in their own illustration the patient's symptoms shifted from the respiratory system to the gastrointestinal system. I know of cases in which this shifting of the disease has affected not two, but three or even four systems in succession. I consider this shifting of symptoms from one system to another a very characteristic or even pathognomonic feature of the syndrome.

My experience leads me to suspect that this syndrome is really infectious in nature and traceable to some virus or fungus. I note that Ruzic and his associates tested the patient for viral or fungal infection only once. It would be interesting to know what the results would have been if the tests had been made repeatedly, as in the case of the stool examination. The final checkup of the patient, too, was done only once and that eight months after the operation, when his eosinophil count was normal. I have seen cases in which the eosinophil count after remaining low for a time goes up substantially and also cases in which the symptoms after an interval of quiescence have flared up again, months and even years later, or have passed on to another physiological system. It is definitely worth while therefore to follow up the examination of such patients over a period of decades. I intentionally use the word decades, because I have a vague suspicion, based on the detailed history of some of my patients, that in many cases the disease runs out its course in the period of one or two decades.

My studies on Loeffler's syndrome also incline me to the view that a transition from a readily reversible to a less easily reversible or even an irreversible hypersensitive histological sequence (as demonstrated in the experiments of Arthus) can and does occur in some cases of this disease, contrary to popular notions about it.

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# MEDICAL MOTION PICTURES

**A Concept of Maternal and Neonatal Care:** 16 mm., black and white, sound, showing time 25 minutes. Prepared by Preston A. McLendon, M.D., and John Parks, M.D., George Washington University School of Medicine. Produced in 1951 by Washington University School of Medicine and the Medical Audio-Visual Institute. Procurable on rental ($5.00) or purchase ($50.00) from Medical Audio-Visual Institute, 185 N. Wabash Ave., Chicago.

This film demonstrates a concept of care that starts with the first prenatal visit and extends through delivery, hospital stay, and return home with a new baby. The related duties of the medical team of obstetrician, pediatrician, nurses, and hospital administrator are illustrated to show the influence they have on the health, confidence, and comfort of all members of the family. In the hospital portion of the film, emphasis is placed on a balance of scientific facilities, educational experiences, and homelike accommodations (rooming-in). A variety of room and nursery arrangements are illustrated; however, physical facilities, while convenient, are not essential to the way of practice shown in the film.

This motion picture represents a report to the medical profession of an idea or a method of practice. The authors have illustrated some of the features of what they consider coordinated obstetric and pediatric care as they center around a hospital practice. It is not meant to be an instructional film on techniques. Some of the concepts presented by the authors are controversial, and a picture of this kind should provoke considerable discussion. It is suitable for showing to physicians, nurses, and hospital administrators. The film is well organized and directed, and the photography is excellent.

**Surgical Approaches to the Hip Joint:** 16 mm., color, sound, showing time 35 minutes. Produced in 1951 for the Veterans Administration by Churchill-Wexler Productions, Los Angeles. Leroy C. Abbott, M.D., University of California Medical School, Technical Adviser. Procurable on loan from Central Office Film Library, Motion Picture Service, Office of Information, U. S. Department of Agriculture, Washington 25, D. C.

This motion picture shows three of the most commonly used surgical approaches to the hip joint, namely, the anterior approach, the posterior approach, and the lateral approach for nailings of the hip. Through reiteration of anatomy concerning the hip, including the superposition of the animated drawings on the anatomy, anyone reviewing or seeing this film will have a clear idea of the pitfalls to be avoided and the care that has to be taken in obtaining the proper approach. The film is as instructive to the skilled surgeon as it is to the student who is first coming in contact with anatomy. To the latter, it could not help but be an inspiration to learn and appreciate what this subject will mean to him in the future. The photography, animation, and every phase of the production of this film are excellent. It is highly recommended for the teaching, study, and review of anatomy of the hip joint.

## NEW FILM ADDED TO A. M. A. MOTION PICTURE LIBRARY

**The Picture of Health:** 16 mm., black and white, sound, showing time 13 minutes. Produced in 1952 by Herman Ellis, Michigan Pictures, Lansing, for the Michigan Health Council. Procurable on loan (service charge $2.00) from Committee on Medical Motion Pictures, American Medical Association, 535 N. Dearborn St., Chicago 10.

This film uses the problem solving approach in its illustration of health council organization. It shows a community with a health problem, the seeking of a means for solving that problem, the ultimate development of a health council, and the solution of their particular problem through the cooperative effort of the newly organized health council and other community organizations. The locale in this film is so planned that the mythical town of Pleasantville might be located in any state. This film would be of particular value to high school classes in civics, social studies, and community problems; local governmental bodies, voluntary health organizations, and citizen groups concerned with the solution of community health problems. The photography and narration are satisfactory.

# BUREAU OF LEGAL MEDICINE AND LEGISLATION

## MEDICOLEGAL ABSTRACTS

**Medical Practice Act: Constitutionality as Applied to Chiropractors.**—Defendant chiropractors held themselves out to the public as being skilled in the science of healing the sick by manual pressure applied to the body of the patient and the use of heat lamps and electric massage. They were found guilty in the trial court of practicing medicine without a license, so they appealed to the Supreme Court of Louisiana.

The defendants contended that they were not practicing medicine and that if they were they did not require a license because the medical practice act is unconstitutional. At the outset, said the Supreme Court, it is pertinent to state that this court has heretofore ruled twice that the practice of chiropractic is that of the practice of medicine and that the medical practice act is impregnable to the charge that it violates the equal protection clause of the 14th Amendment of the Constitution or that it denies to chiropractors due process. The chiropractors in this case, however, sought to evade the effect of these adjudications by arguing that the concept of the practice of medicine as defined by the medical practice act has been markedly curtailed since the two cases were decided and that, specifically, the legislature, by passage of the osteopathic act, modified the general definition to exclude therefrom chiropractors and others who treat by the application of physical pressure.

We are unable to perceive merit in this proposition, said the Supreme Court. The medical practice act as amended is a broad and all-inclusive statute covering the entire field of the healing art in this state, and the practice of medicine as defined therein embraces every known type or method of treatment for the relief or cure of ailments or disease. The practices of osteopathy, dentistry, and optometry, like that of chiropractic, fall within the scope of the act; and osteopaths, dentists, and optometrists would be amenable to its provisions but for the exemption that the legislature has seen fit to grant them when they are legally licensed to practice in their respective fields. Hence, by specially defining the practice of osteopathy, the legislature neither intended to, nor did it, contract the definition of the practice of medicine so as to exclude therefrom the type of healing practiced by the defendants.

The defendants also contended that the medical practice act is unconstitutional because it discriminates in favor of legally licensed osteopaths, dentists, and so forth. There can be no denial that the regulation of the practice of medicine is within the police power of the state. The legislature in its wisdom also has the right to exempt certain persons or classes of persons from the provisions of a law, provided that there is no arbitrary or unreasonable discrimination, and a statutory discrimination will not be set aside as a denial of the equal protection of the laws "if any state of facts reasonably may be conceived to justify it." There is no showing whatever in this case to overcome the presumption that the legislature had just and reasonable grounds for exempting licensed osteopaths, dentists, and optometrists from the provisions of the medical practice act.

Likewise without substance is the defendants' contention that the act confers arbitrary powers on the medical board and thus denies equal protection. The alleged arbitrary powers of the board are said to be contained in section 2 of the act declaring that, before any person may enter the practice of medicine, he shall present to one of the boards of medical examiners "a diploma from a college in good standing, of any sect teaching medicine or the healing art, and shall stand a satisfactory examination. . . ." It is asserted that since the medical board is given the right to determine what is or what is not "a college in good standing" the statute vests in it arbitrary power that may be and actually has been exercised in the interest of a favored few. The requirement that the applicant present a diploma from a college in good standing does not clothe the board with an

arbitrary power but only with the right to exercise discretion; what is or what is not a college in good standing is a matter for determination by the board after investigation, but, should it refuse an examination to an applicant presenting a diploma from a reputable medical school, its action would then be regarded as arbitrary and subject to coercion by mandamus. The possibility of arbitrary action, where discretion is vested in an administrative body, does not render the statute vulnerable to the charge that it denies an equal protection of the laws.

It is next argued that the act denies equal protection because the medical board has unreasonably imposed an educational requirement that an applicant for examination produce a diploma from a college recognized by the American Medical Association. This point is said to be founded on the testimony of Dr. Roy B. Harrison, Secretary of the Board of Medical Examiners. While we do not understand that Dr. Harrison stated that only applicants with diplomas from colleges recognized by the American Medical Association will be favorably considered by the board, said the Supreme Court, it would make no difference insofar as the constitutionality of the act is concerned whether the board has taken such a stand or not. If the board has made an arbitrary ruling as to the colleges that it recognizes as being in good standing, the remedy of the injured party is to apply for a mandamus.

Accordingly, the judgments of conviction against the defendant chiropractors were affirmed. *Louisiana State Board of Medical Examiners v. Beatty, 55 So. (2d) 761 (Louisiana, 1951).*

# COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

## ADDITIONAL HOSPITALS REGISTERED

The following hospitals were registered by the Council on Medical Education and Hospitals of the American Medical Association at its meeting in Denver, Colo., Dec. 1, 1952.

Elkourie Clinic and Hospital, Birmingham, Ala.
Bullock County Hospital, Union Springs, Ala.
Ouachita County Hospital, Camden, Ark.
Hot Spring County Memorial Hospital, Malvern, Ark.
Magnolia Park General Hospital, Burbank, Calif.
Calexico Hospital, Calexico, Calif.
Foothill Convalescent Hospital, Campbell, Calif.
Modoc Medical Center (Two Units), Cedarville & Alturas, Calif.
Enloe Hospital, Chico, Calif.
Desert Hospital, Palm Springs, Calif.
Marin General Hospital, San Rafael, Calif.
Ft. Morgan Community Hospital, Ft. Morgan, Colo.
Nanticoke Memorial Hospital, Seaford, Del.
Everglades Memorial Hospital, Pahokee, Fla.
Gadsden County Hospital, Quincy, Fla.
Sunhaven, St. Petersburg, Fla.
West Orange Memorial Hospital, Winter Garden, Fla.
Marioni Convalescent Home, Augusta, Ga.
Appling General Hospital, Baxley, Ga.
Rabun County Memorial Hospital, Clayton, Ga.
Habersham County General Hospital, Demorest, Ga.
St. Luke's Hospital, Macon, Ga.
McRae-Telfair County Hospital, McRae, Ga.
Jasper Memorial Hospital, Monticello, Ga.
Chattooga County Hospital, Summerville, Ga.
Winder-Barrow Hospital, Winder, Ga.
St. Benedict's Hospital, Jerome, Idaho
Villa Terrace Convalescent Home, Alton, Ill.
Doctors Hospital, Carbondale, Ill.
Carlinville Area Hospital, Carlinville, Ill.
Rock Island County Convalescent Home, Coal Valley, Ill.
Mt. Vernon State Tuberculosis Sanit., Mt. Vernon, Ill.
Beverly Shores Rest Home, Beverly Shores, Ind.
Grace Convalescent Home, Fort Wayne, Ind.
Hancock County Memorial Hospital, Greenfield, Ind.
Larue D. Carter Memorial Hospital, Indianapolis, Ind.
Dr. Norman B. Beatty Memorial Hospital, Westville, Ind.
Crawford County Memorial Hospital, Denison, Iowa
Veterans Admin. Hospital, Iowa City, Iowa
Comanche County Hospital, Coldwater, Kan.
Lincoln County Hospital, Lincoln, Kan.
Logan County Hospital, Oakley, Kan.
Trigg County Hospital, Cadiz, Ky.
Corbin Municipal Hospital, Corbin, Ky.
Mayfield Hospital, Mayfield, Ky.
Bourbon County Hospital, Paris, Ky.
Allen County War Memorial Hospital, Scottsville, Ky.
Guerrant Clinic and Hospital, Winchester, Ky.
Huckabay Clinic and Hospital, Coushatta, La.
DeSota General Hospital, Mansfield, La.
Russell Hospital, Brewer, Maine
Doctors Hospital, Baltimore, Md.
Veterans Admin. Hospital, Baltimore, Md.
Veterans Admin. Hospital, Boston, Mass.
Deckerville Hospital, Deckerville, Mich.
Barlow Hospital, Detroit, Mich.
St. John Hospital, Detroit, Mich.
Paul Oliver Memorial Hospital, Frankfort, Mich.
Otsego County Memorial Hospital, Gaylord, Mich.
Marlette Community Hospital, Marlette, Mich.
Northville State Hospital, Northville, Mich.
Greenbush Community Hospital, Greenbush, Minn.
Meeker County Memorial Hospital, Litchfield, Minn.
Stevens County Memorial Hospital, Morris, Minn.
Renville County Hospital, Olivia, Minn.
Pelican Valley Health Center, Pelican Rapids, Minn.
St. John's Hospital, Red Lake Falls, Minn.
House-Carlson Clinic-Hospital, Batesville, Miss.
Jones County Community Hospital, Laurel, Miss.
Noxubee General Hospital, Macon, Miss.
Beacham Memorial Hospital, Magnolia, Miss.
North Sunflower County Hospital, Ruleville, Miss.
Veterans Admin. Hospital, Kansas City, Mo.
Mountain View Memorial Hospital, Mountain View, Mo.
Alma Memorial Hospital, Alma, Neb.
Atkinson Memorial Hospital, Atkinson, Neb.
Antelope Memorial Hospital, Neligh, Neb.
Saunders County Community Hospital, Wahoo, Neb.
Memorial Hospital, Woodbury, New Jersey
San Juan Hospital, Farmington, N. Mex.
Bainbridge Hospital, Bainbridge, N. Y.
Benedict Memorial Hospital, Ballston Spa, N. Y.
Hebrew Home and Hospital for Chronic Sick, New York City, N. Y.
Pender Memorial Hospital, Burgaw, N. C.
North Carolina Memorial Hospital, Chapel Hill, N. C.
Good Samaritan Hospital, Charlotte, N. C.
Keeley Institue, Greensboro, N. C.
Highlands Community Hospital, Highlands, N. C.
Kings Mountain Hospital, Kings Mountain, N. C.
Wilkes General Hospital, North Wilkesboro, N. C.
Johnston Memorial Hospital, Smithfield, N. C.
Bertie County Memorial Hospital, Windsor, N. C.
Lula Conrad Hoots Memorial Hospital, Yadkinville, N. C.
Tri-State Memorial Hospital, Bowman, N. D.
Garrison Memorial Hospital, Garrison, N. D.
Community Memorial Hospital, Lisbon, N. D.
Brown County General Hospital, Georgetown, Ohio
Eugene H. Hughes Memorial Hospital, Hamilton, Ohio
Highlands Community Hospital, Hillsboro, Ohio
Memorial Hospital, Maryville, Ohio
Williams County General Hospital, Montpelier, Ohio
Greene Memorial Hospital, Xenia, Ohio
Watonga Municipal Hospital, Watonga, Okla.
Curry General Hospital, Gold Beach, Ore.
Pioneer Memorial Hospital, Prineville, Ore.
Central Oregon District Hospital, Redmond, Ore.
Raymond Private Hospital and Nursing Home, Johnstown, Pa.
Olney Hospital and Lawncrest Diagnostic Clinic, Philadelphia, Pa.
Veterans Admin. Hospital, Philadelphia, Pa.
Angelus Convalescent Hospital and Nursing Home, Pittsburgh, Pa.
Lee County Memorial Hospital, Bishopville, S. C.
Allendale County Hospital, Fairfax, S. C.
Allen Bennett Memorial Hospital, Greer, S. C.
Five Counties Hospital, Lemmon, S. D.
Whiting Memorial Clinic and Hospital, Woonsocket, S. D.
Brint Hospital, Bolivar, Tenn.
Doyle Currey Clinic-Hospital, Chattanooga, Tenn.
Tennessee Tuberculosis Hospital, Chattanooge, Tenn.
Speck Hospital, Cleveland, Tenn.
Collins Chapel Connectional Hospital, Memphis, Tenn.
Le Bonheur Children's Hospital, Memphis, Tenn.
Fayle Clinic and Hospital, Baytown, Texas
Beaumont Infirmary, Beaumont, Texas
Bowie Clinic Hospital, Bowie, Texas
Cleburne Hospital, Cleburne, Texas
Allen Hospital, Commerce, Texas
Allen Memorial Hospital, Commerce, Texas
W. I. Cook Memorial Hospital Center for Children, Ft. Worth, Texas
Hanna Hospital, Glen Rose, Texas
Medina Hospital, Hondo, Texas
Memorial Hospital, Palestine, Texas
Pasadena Hospital and Clinic, Pasadena, Texas
Sunland Convalescent Home, San Benito, Texas
Stromberg Clinic and Hospital, Taylor, Texas
Swisher County Hospital, Tulia, Texas
Baker Clinic-Hospital, Wills Point, Texas
Juab County Hospital, Nephi, Utah
Veterans Admin. Hospital, Salt Lake City, Utah
Giles Memorial Hospital, Pearisburg, Va.
Richmond Eye, Ear, Nose and Throat Hospital, Richmond, Va.
Franklin Memorial Hospital, Rocky Mount, Va.
Grays Harbor Community Hospital, Aberdeen, Wash.
Kennewick General Hospital, Kennewick, Wash.
Good Samaritan Hospital, Puyallup, Wash.
Skyline Hospital, White Salmon, Wash.
Marmet Hospital, Marmet, W. Va.
Memorial Hospital, Darlington, Wis.
U. S. Air Force Hospital, Elmendorf, Alaska
Hospital Hato Tejas, Bayamon, P. R.
Vasquez Trelles Clinic Hospital, Santurce, P. R.

# MEDICAL LITERATURE ABSTRACTS

## UNITED STATES

### A.M.A. Arch. of Dermat. and Syphilol., Chicago

66:427-546 (Oct.) 1952

Modes of Spread of Cancer of Skin. F. E. Mohs and T. G. Lathrop. —p. 427.
German Schools of Dermatology in the Past Century. H. M. Buley —p. 440.
Original Description of Lupus Erythematosus. E. Gahan.—p. 458.
Secondary Eruptive Xanthomatosis Due to Myxedema: Genetic and Metabolic Study. A. C. Curtis and H. C. Blaylock.—p. 460.
*Pilonidal Sinus of Hand. M. Waisman and R. G. Olivetti.—p. 466.
Further Studies of Mosaic Fungus. E. S. Dowding.—p. 470.
*Chronic Ulcers of Leg Associated with Blood Dyscrasia. F. Pascher and R. Keen.—p. 478.
Natural Steroid Complex ("Marisone") in Treatment of Cutaneous Diseases. A. D. Spielman and A. Blau.—p. 488.
Anaphylaxis from Penicillin: Report of Case. G. M. Stroud.—p. 491.
Erythema Gyratum Repens: Skin Manifestations in Patient with Carcinoma of Breast. J. A. Gammel.—p. 494.
Intracutaneous Hyaluronidase Action in Normal and Roentgen-Irradiated Rabbits: Histological Study. H. B. Praytor.—p. 506

**Pilonidal Sinus of Hand.**—A case of an interdigital sinus and hair-containing granuloma on the hand of a barber is described. The lesion, produced by the occupational penetration of extraneous hairs into the skin, is literally "pilonidal," made up of the embedded hairs and the product of reaction of the surrounding tissue. Clinical features of the disease and observations regarding its pathogenesis are reviewed. Lesions are usually single, affecting any interdigital space on either hand. Pathologically, a sinus and/or an abscess or a foreign body granuloma or combinations of these are produced about the heterogenous hairs. Treatment consists of either total excision or incision and curettage of the diseased tissue.

**Chronic Ulcers of Legs Associated with Blood Dyscrasia.**—Pascher and Keen call attention to the role of blood dyscrasias in the pathogenesis of chronic ulcers of the lower extremities. They present the histories of five patients: a case of sickle cell anemia in which leg ulcers appeared later in life than in most cases hitherto reported; a case of familial hemolytic jaundice associated with arteriosclerosis obliterans, in which one of the ulcers ultimately gave rise to a prickle cell epithelioma; a case of Mediterranean disease (Cooley's anemia), with recurrent ulcers of the legs; a case of symptomatic polycythemia associated with a leg ulcer; and a case of polycythemia vera associated with a leg ulcer and multiple ulcerations of the skin. In the patient with polycythemia vera it was thought that malnutrition or trophic disturbances secondary to nervous system involvement were probable causes of ulceration of the leg. In the patient with symptomatic polycythemia secondary to pulmonary fibrosis, the leg ulcer was attributable to thrombophlebitis of the superficial veins. The authors discuss various hypotheses advanced to explain the association of leg ulcers with blood dyscrasias.

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Titles marked with an asterisk (*) are abstracted.

### A.M.A. Arch. Internal Medicine, Chicago

90:425-576 (Oct.) 1952

*Hypochloremic Alkalosis Induced by Mercurial Diuretics in Congestive Heart Failure: Reversible Form of So-Called Refractory Heart Failure. J. F. Stapleton and W. P. Harvey.—p. 425.
Controlled Hypoxemia Test for Coronary Insufficiency Employing the Millikan Oximeter: Study of Normal and Abnormal Responses. H. E. Tewell Jr. and J. S. Pritchard.—p. 435.
*Residual Effects of Rickettsial Disease on Central Nervous System: Results of Neurologic Examinations and Electroencephalograms Following Rocky Mountain Spotted Fever. M. J. Rosenblum, R. L. Masland and G. T. Harrell.—p. 444.
Histoplasmosis: Three Fatal Cases with Disseminated Sarcoid-Like Lesions. H. Pinkerton and L. Iverson.—p. 456.
*Acute Diffuse Interstitial Fibrosis of Lungs. W. P. Callahan Jr., J. C. Sutherland, J. K. Fulton and J. R. Kline.—p. 468.
Porphyria Cutanea Tarda: Investigation of Case, Including Isolation of Some Hitherto Undescribed Porphyrins. A. G. Macgregor, R. E. H. Nicholas and C. Rimington.—p. 483.
Observations on Alleged Serotonin- (Enteramine)-Like Nature of Cerebral Pressor Substance of Taylor, Page, and Corcoran. V. Erspamer. —p. 505.
Recent Advances in Nutrition and Metabolism: Review of Literature, 1951. G. A. Goldsmith, W. G. Unglaub and J. Gibbens.—p. 513.

**Hypochloremic Alkalosis Induced by Mercurial Diuretics.**—Four patients with congestive heart failure who had been treated with mercurial diuretics for years became refractory to these diuretics. This refractory state was due to a disturbance of electrolyte balance that produced hypochloremic alkalosis. This differs from the low-salt syndrome in several important respects. The carbon dioxide combining power is normal or elevated, the serum sodium usually remains normal, and azotemia is not ordinarily present. The authors' patients recovered their response to mercurial diuretics following a high chloride intake without the addition of sodium. Ammonium chloride was administered in doses of 6 to 8 gm. by mouth daily. The patients were also given 4 cc. of 10% hydrochloric acid solution diluted in a glass of water four times daily. The hypochloremic alkalosis syndrome is emphasized as a frequent but not well-publicized complication of the use of mercurial diuretics. The relative ease of diagnosis and treatment makes its consideration mandatory in every case of refractory heart failure. Hypochloremic alkalosis is only one facet of refractory congestive heart failure, but its recognition may be life-saving.

**Rickettsial Disease and Central Nervous System.**—Of 56 patients of all ages who had been successfully treated for Rocky Mountain spotted fever, 37 were reexamined one to eight years after the acute phase of the illness, while 19 could not be traced. Of the 37 patients 21 had some type of neurological sequelae. Fourteen patients gave a history of symptoms related to the central nervous system, 6 had neurological signs, and 12 had clearly abnormal electroencephalograms. Twelve additional patients had borderline electroencephalographic abnormalities. The electroencephalogram was abnormal in a high proportion of patients who had had fever for more than 10 days. Of 15 patients who had been observed to have abnormal neurological signs during the acute illness, 3 had residual signs, and 2 were having convulsions. Seven of the 15 patients had abnormal electroencephalograms, 4 had borderline tracings, and 4 showed no electroencephalographic changes. Of 24 patients who received supportive therapy alone, including those treated with antiserum or paraaminobenzoic acid, 14 had neurological sequelae of some sort; these sequelae were severer than those observed in patients who received antibiotic therapy. Of the 13 patients treated with antibiotics, 6 had evidences of residual neurological damage. Only one of seven patients who received antibiotics within the first three days of rash had an abnormal electroencephalogram. Necropsy was performed on eight patients who died during the acute illness. Microscopic evidence of damage was found in all

six patients in whom the brain was examined. In these patients microinfarcts or granulomas were found adjacent to cerebral blood vessels. It is concluded that damage to the central nervous system is common in spotted fever. In some patients the acute changes are reversible with convalescence; in others residual damage persists longer than a year and may be assumed to be permanent.

**Acute Interstitial Fibrosis of Lungs.**—A case of acute interstitial fibrosis of the lungs in a 55-year-old white man is reported. Cough, hemoptysis, and dyspnea with progressing cyanosis were the presenting symptoms. Roentgenograms showed progressive dissemination of peribronchial densities, which began at the base of the lungs and extended to all lobes in two weeks. An area of alveolar consolidation was observed in the axillary segment of the right upper lobe. The rapid progressive increase in density to involve all lobes of the lungs was undoubtedly a result of the interstitial fibrosis but may partly be a result of the accumulation of fibrinous material in the alveolar spaces. Treatment was started with potassium iodide and cortisone without improvement in the patient's condition. Penicillin, chloramphenicol, and streptomycin were also ineffective. The chest remained hyperresonant and free from rales. The sputum still contained streaks of blood but remained free of purulent material, indicating the absence of suppurative inflammation in the tracheobronchial tree. Dyspnea and cyanosis gradually became severer, and the patient died on the 27th hospital day after an illness of three and a half months' duration. At necropsy there was no fluid in the pleural cavities and no exudate on the surfaces of the visceral pleura. The lungs showed a diffuse increase in interstitial connective tissue with proliferation of young fibroblasts within the alveolar septa and in the perivascular and peribronchial regions. The alveolar spaces were filled with a fibrinous material. The fibrin in the center of the alveoli was deeply eosinophilic and finely granular without a reticular structure. Radiating from this central zone were stellate fibrinous strands forming an interlacing pattern. There was no cellular infiltration of an inflammatory type either in the alveoli or in the interstitial tissue. The extensive deposition of fibrinous material within the alveoli without anatomical evidence of an exudative process indicated terminal pulmonary edema and transudation of a fluid high in protein content into the alveolar spaces. The clinical signs, symptoms, and roentgenologic findings in the authors' case were analogous to those in 15 cases previously reported by other workers. The pathological changes in the lungs were similar except for the accumulation of fibrinous material in the alveolar spaces. The complete lack of cellular infiltration implies that the basic lesion of interstitial fibrosis is not bacterial and if inflammatory must be a result of virus infection. Changes in the lungs similar to lymphedema seen in other tissues suggested chronic pulmonary lymphedema as a possible etiological factor. The cause, however, remains obscure, and further studies are needed.

## A.M.A. Arch. Ophthalmology, Chicago

**48:271-392 (Sept.) 1952**


*Association of Uveal Nevi with Skin Nevi. A. B. Reese.—p. 271.
Further Efforts to Influence X-Ray Cataract by Chemical Agents. L. von Sallmann.—p. 276.
Leptospiral Uveitis: Report of Bacteriologically Verified Case. A. Alexander, A. Baer, J. R. Fair and others.—p. 292.
Ocular and Subcutaneous Inflammatory Responses to Transplantation of Heterologous Tumors. A. C. Snell Jr.—p. 298.
Use of Typhoid Vaccine in Continuous Intravenous Infusion in Treatment of Eye Diseases. R. Buxeda.—p. 307.
Ocular Findings in Scrub Typhus. W. P. Chamberlain Jr.—p. 313.
Dacryocystorhinostomy in Infants and Children. S. S. Blankstein.—p. 322.
Ocular Involvement in Lymphomatous Disease. A. R. Feinstein and A. C. Krause.—p. 328.
Pathogenesis of Intraocular Hypertension in Cases of Arteriovenous Aneurysm. R. Weekers and Y. Delmarcelle.—p. 338.


**Association of Uveal Nevi with Skin Nevi.**—Reese calls attention to the frequent association of iris nevi with ipsilateral skin nevi. He has seen this association often enough to feel that it is not accidental and that it may sometimes be clinically useful in indicating the true nature of a pigmented lesion of the iris. He describes four cases in which elevated, well-localized, pigmented tumors occurred in the periphery of the iris in association with skin nevi. In two of the four patients there were freckles on the affected iris and none on the other iris. In two additional cases, a nevus-like melanoma of the iris was associated with a nevus of the margin of the lower lid of the other eye. One choroidal lesion that may have been a nevus was observed in association with an extensive ipsilateral pigmented nevus of the skin of the head and eyelids. These observations seem to suggest that when a pigmented lesion of the iris is associated with excessively numerous or large ipsilateral skin nevi it is likely to be a nevus.

## American Journal of Human Genetics, Baltimore

**4:155-232 (Sept.) 1952. Partial Index**


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Linkage Tests of Mediterranean Anemia with Blood Groups, Blood Types, Rh Factors and Eye Color. I. Ludwin, D. Limentani and W. Dameshek.—p. 182.
Absence of Linkage Between the Genes Responsible for the Sickling Phenomenon, the MN Blood Types, and S-Agglutinogen. J. V. Neel, W. J. Schull and H. S. Shapiro.—p. 204.


## American Journal of Medical Sciences, Philadelphia

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*Heritage of Hypertension. C. B. Thomas.—p. 367.
*Effect of Theophylline with Ethylenediamine (Aminophylline) and Caffeine on Cerebral Hemodynamics and Cerebrospinal Fluid Pressure in Patients with Hypertensive Headaches. J. H. Moyer, A. B. Tashnek, S. I. Miller and others.—p. 377.
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*Treatment of Rheumatic Fever with ACTH. I. Smaller Doses of ACTH in Acute Rheumatic Fever. J. A. Sheinkopf, G. C. Griffith, R. Morrison and P. Starr.—p. 390.
Id.: II. ACTH by Continuous Intravenous Drip Method. G. C. Griffith, J. A. Sheinkopf, J. D. McNair and P. Starr.—p. 397.
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Evaluation of Vasodilator Drugs in Four Patients with Arteriosclerosis Obliterans. E. C. Texter Jr., W. Redisch, E. Sheckman and others.—p. 408.
Electrocardiographic Changes Associated with Hypercalcemia and Hypocalcemia. P. N. G. Yu.—p. 413.
Electrocardiographic Criteria of Left Ventricular Hypertrophy. W. I. Heine, C. F. Sackett and W. Serber.—p. 424.
Clinical Effectiveness of Certain of Hydrogenated Alkaloids of Ergot in Peripheral Vascular Disorders. J. E. Roberts, L. L. Anderson and T. M. Parry.—p. 431.
Vitamin K Control of Increased Hypoprothrombinemic Effect of Dicumarol in Congestive Heart Failure. D. F. Covert.—p. 439.
Penicillin Treatment of Cardiovascular Syphilis. H. Beerman.—p. 446.
Tracheotomy in Bulbar Poliomyelitis: Review. A. H. Neffson.—p. 465.


**Inheritance of Hypertension.**—The circulatory pattern of 84 medical students at Johns Hopkins University who had a history of hypertension in one or both parents were compared with those of 100 control persons whose parents were both free from hypertension. Results showed that circulatory lability is more prevalent among the offspring of hypertensive than among those of nonhypertensive parents. Where a significant correlation with parental hypertension exists, such lability is usually demonstrable in a number of different ways. The heart as well as the blood pressure frequently participates in the pattern of lability. In the entire group the percentage of persons showing circulatory lability was higher than the incidence of hypertension in the parents' generation, suggesting that additional factors are necessary for the appearance of hypertension. Preliminary genetic analysis indicates that hypertension bears an etiological relationship to coronary artery disease and that the same heritage is expressed oftener as hypertension in women and as coronary artery disease in men. While in some respects hypertension appears due to a single recessive gene widely distributed in the population, it seems probable that a more complex genetic pattern is involved.

**Aminophylline and Caffeine in Hypertensive Headaches.**—Six patients with hypertensive headaches were treated with aminophylline, four were treated with caffeine, and three received first one drug and then the other for comparison of the effects pro-

duced. Cerebral blood flow determinations were performed before and after the intravenous administration of 0.5 gm. of aminophylline or caffeine and sodium benzoate in 50 cc. of isotonic sodium chloride solution. Cerebrospinal fluid pressure readings were taken at a later date, employing the same method of drug administration. Both aminophylline and caffeine caused prompt relief of headaches resulting from the hypertensive state. Aminophylline proved to be the more effective agent in this respect. The presence of kidney disease or heart failure did not alter this response. The authors' data suggest that caffeine and aminophylline decrease the arterial and postarteriolar vascular distention of the cerebral vessels and thus relieve the headache. If relief is to be anticipated, it is necessary to determine that the headache is due to the hypertension and not to some unrelated cause. Both aminophylline and caffeine caused an increase in cerebrovascular resistance, with a decrease in cerebral blood flow. This was followed by a fall in spinal fluid pressure. Therefore, aminophylline is an effective agent for acutely reducing cerebrospinal fluid pressure in patients with hypertension. The fall in cerebrospinal fluid pressure is secondary to a decrease in cerebral blood flow.

**Benzpyrinium Bromide in Early Pregnancy and Delayed Menstruation.**—Benzpyrinium ("stigmonene") bromide, a new cholinergic agent, was given intramuscularly in doses of 1 cc. of a 1:1,000 solution (1 mg.) on three successive days to 100 women with delayed menstruation. None of these women had previous menstrual irregularities, evidence of menopause, organic pelvic disease, or causative endocrine or constitutional disturbance. In 83 of the 100 women, the drug did not evoke the menstrual flow after the last injection, and they were, therefore, considered pregnant. The diagnosis of pregnancy was established clinically in each, and in all but one instance was confirmed by the Aschheim-Zondek test. The test had no apparent harmful effects on gestation. Sixteen of the remaining 17 women who were amenorrheic for an average of 20.1 days were considered not pregnant clinically. These had negative Aschheim-Zondek tests and menstruated within 2 to 120 hours following the last injection of benzpyrinium bromide. The therapeutic efficiency of this drug in simple delayed menstruation thus was 94.1%. No instance of drug reaction or sensitivity was observed.

**Corticotropin in Rheumatic Fever.**—Corticotropin (ACTH) in doses of 0.4 mg. per kilogram of body weight, divided into four equal portions, was administered intramuscularly every six hours to 12 patients with acute and mild rheumatic fever. The dose averaged 5 mg. every six hours for children and 6 mg. every six hours for adults. The duration of therapy varied from 4 to 32 days, 10 of the 12 patients being treated for 18 to 22 days. Eight had carditis, 10 had arthritis, and 3 had skin lesions. Under therapy, fever, arthritis, and skin lesions disappeared rapidly and completely. Gallop rhythm, which was present in three patients, disappeared in seven days. Apical systolic murmurs in three patients diminished or disappeared during hospital observation. Tachycardia persisted for two to four weeks. The white blood cell count rose during treatment and declined abruptly at cessation of therapy. The eosinophil count tended to be low before therapy, remained low during therapy, and returned to a normal level following therapy. The erythrocyte sedimentation rate returned to normal. On withdrawal of corticotropin, a so-called rebound phenomenon was noted in two patients who had moderately severe active rheumatic fever, with a rise in the sedimentation rate and return of symptoms. Reinstitution of corticotropin therapy resulted in a prompt loss of symptoms and a return of the sedimentation rate to normal within 10 days. Thus, small doses of corticotropin as well as short duration of treatment were found to be inadequate for the treatment of active rheumatic fever of moderate severity. The authors' patients were followed for 14 to 22 months. To date, all patients are in the quiescent phase of rheumatic fever and have no evidence of newly acquired valvular disease or aggravation of preexisting valvular disease. While corticotropin cannot be said to cure the disease, it definitely shortens the course.

## American Journal of Surgery, New York

84:381-502 (Oct.) 1952

Retrocaval Ureter: Report of Case and Review of Literature. B. S. Abeshouse and L. H. Tankin.—p. 383.
Progress vs. Perpetuation of Error Concerning Origin of Pregnancy Toxemia. J. Hofbauer.—p. 394.
*Lipomatous Retroperitoneal Tumors. J. H. DeWeerd and M. B. Dockerty. —p. 397.
Carcinoma of the Gallbladder and Bile Ducts. M. A. Howard.—p. 408.
Primary Neurogenic Sarcoma of the Gallbladder. J. Rabinovitch and S. Trinidad.—p. 415.
Paralytic Ileus from Peritonitis After Appendicitis. T. B. Noble.—p. 419.
Interruption of All Arterial Blood Supply to Liver not Compatible with Life: Experimental Study. H. L. Popper and H. Necheles.—p. 429.
Modified Thoracoplasty Performed with Pulmonary Resection. C. W. Lester.—p. 432.
Arterial Transfusion. R. S. Wilson, F. T. Wallace and J. A. Whiting. —p. 436.
Intravenous Anesthesia in Major Obstetric and Gynecologic Surgery: Report of 1,301 Cases. V. P. Mazzola, N. J. Mazzola and L. Pico. —p. 439.
Hourglass Tumors of the Spine in Children: Report of Five Cases. W. R. Chambers.—p. 443.
Treatment of Trochanteric Femoral Fractures with Special Reference to Complications. M. Moore Jr.—p. 449.
Traction-Manipulation for Injuries to the Cervical Spine. W. Klingensmith.—p. 453.
So-Called Trigger Points. B. Judovich and W. Bates.—p. 457.

**Lipomatous Retroperitoneal Tumors.**—The impression prevails that fatty tumors originating in the retroperitoneal space are as innocuous as most other lipomatous tumors. To verify this, DeWeerd and Dockerty studied the 43 cases of primary lipomatous tumor of the retroperitoneal space in which surgical treatment was carried out at Mayo Clinic from 1910 through 1946. In each case, a complete history and the results of general physical examination as well as laboratory data had been recorded. Tissue removed at operation, either the whole tumor or part of it or a biopsy specimen, was available for further gross examination, section, and microscopic study. Follow-up information was obtained in subsequent examinations and from the patient, relatives, or family physician. Studies in the 43 cases revealed that in 28 the tumors were malignant liposarcomas and 15 were benign lipomas. The authors stress the following factors regarding retroperitoneal lipomatous tumors: They may reach astounding size; in one case a 69 lb. (31.3 kg.) fibrolipoma had developed over 17 years. These tumors usually cause few disturbing or alarming symptoms. A urographic survey is the greatest single aid to accurate diagnosis. The treatment of choice is surgical extirpation. About two-thirds of these tumors are malignant. Of the surgically treated patients, 70% showed evidence of recurrence, and in 60% death followed within five years, usually as a result of recurrence. Six of nine patients who survived surgical removal of benign neoplasms are known to have survived beyond a 10 year period.

## Am. Practitioner & Digest of Treatment, Philadelphia

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Rupture of Aortic Valve and Abscesses of Valve Ring Complicating Bacterial Endocarditis: Case Report. E. Abraham and M. M. Jackson. —p. 781.
Present-Day Status of Chemotherapy in Tuberculosis—Clinical Aspects. H. C. Sweany.—p. 785.
Cytologic Examination of Urine, Pleural and Abdominal Fluid. J. M. Blumberg and N. B. Baroody Jr.—p. 791.
Treatment of Herpes Zoster with Chloromycetin. C. S. Wright and J. B. Roxby Jr.—p. 797.
Clinical Studies in Blood Lipid Metabolism. VI. Serial Serum Lipid Partitions in Patients with Chronic Coronary Artery Disease. A. A. Goldbloom.—p. 799.
Myalgia of Isolated Portion of Muscle: Therapeutic Value of Its Recognition. A. Gordon.—p. 804.
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Role of Bracing in Low Back Conditions. O. F. Von Werssowetz.—p. 829.
Treatment of Anorectal Discomfort with Anesthetic Ointment. W. H. Ramsey.—p. 834.

## Antibiotics & Chemotherapy, Washington, D. C.

2:441-494 (Sept.) 1952. **Partial Index**

Some Properties of Magnamycin, a New Antibiotic. F. W. Tanner Jr., A. R. English, T. M. Lees and J. B. Routien.—p. 441.
*Neomycin in Treatment of Urinary Tract Infections. R. M. Nesbit, A. I. Dodson Jr. and C. C. Mackinney.—p. 447.
Actithiazic Acid. IV. Pharmacological Studies. K. Hwang.—p. 453.
Catenulin, a New Antibiotic. J. W. Davisson, I. A. Solomons and T. M. Lees.—p. 460.
Ascosin, an Antifungal Antibiotic Produced by a Streptomycete. R. J. Hickey, C. J. Corum, P. H. Hidy and others.—p. 472.
Relationship of Streptomycin Sensitivity of M. Tuberculosis to Action of Hydrazines of Isonicotinic Acid (Rimifon and Marsalid). M. H. Fusillo, B. M. Wagner and D. M. Kuhns.—p. 484.

**Neomycin in Urinary Tract Infections.**—The new antibiotic neomycin is readily soluble in water and most active in an alkaline medium. It has a wider antibacterial spectrum than bacitracin, streptomycin, or penicillin and is active against both gram-positive and gram-negative organisms. It is not only bacteriostatic but strongly bactericidal. Resistant strains are less likely to develop with use of neomycin than with streptomycin. Although animal experimentation has shown neomycin to possess a relatively low toxicity, clinically it produced both nephrotoxic and ototoxic symptoms when administered in daily doses of 1 to 2 gm. for long periods (up to three months). Nesbit and associates decided to try smaller doses, giving 0.25 gm. intramuscularly every six hours for a maximum of five days. Eighteen patients with chronic urinary tract infections had previously received one to five different therapeutic agents with no appreciable effect. Aerobic urine cultures were obtained prior to therapy, and the offending organism was tested for sensitivity to neomycin, chloroamphenicol, terramycin, and aureomycin. Patients were selected for neomycin therapy on the basis of the sensitivity of the isolated organism to neomycin or because they failed to respond to other agents. Twelve of the 18 patients had conversion of urine to normal, as determined by posttherapy cultures. Eight of these were clinically free from infection when seen from one week to nine months after therapy. In 102 in vitro sensitivity studies, neomycin compared favorably with other, newer antibiotics. In 79 of these studies the organism was sensitive to neomycin, and in 31 studies neomycin could be considered the antibiotic of choice for treatment. Toxic reactions were minimal with low but clinically effective dosage.

## California Medicine, San Francisco

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Clinical Picture of Pancreatic Insufficiency. C. L. Brown.—p. 172.
Pancreatitis and Carcinoma of the Pancreas: Some Aspects of Pathologic Physiology. H. A. Edmondson.—p. 176.
Adenoma of Islets of Langerhans. J. H. Saint.—p. 180.
Operations on the Pancreas: Some Technical Considerations. C. Mathewson Jr.—p. 183.
*Coxsackie Virus in Southern California: Isolation of Strain from Stool of Patient. R. A. Boak, B. F. Klaumann and C. B. Ward Jr.—p. 187.
Abscesses of the Breast: Recurring Lesions in Areolar Area. A. R. Kilgore and R. Fleming.—p. 190.
Complications of Intestinal Intubation with Report of Two Cases of Unusual Complications. I. L. Lichtenstein.—p. 192.

**Coxsackie Virus Isolated from a Patient's Stools.**—Coxsackie virus produces fever, headache, backache, muscle pain and spasm, stiff neck, abdominal pain, nausea, vomiting, pleural pain, sore throat, malaise, and anorexia, the most consistent symptoms being fever and headache. Paralysis occurs in a small percentage of cases. Two clinical syndromes other than that resembling poliomyelitis have been associated with the Coxsackie virus; it has been recovered from patients with so-called epidemic pleurodynia (Bornholm disease) and from patients with herpangina. Stool specimens and paired blood samples were collected from 29 patients at the Long Beach Veterans Administration Hospital, and tentative diagnoses, including aseptic meningitis, nonparalytic poliomyelitis, pneumonitis, and ulcerative colitis, were made. The inoculum from only 2 of 33 stool specimens produced paralysis in suckling mice. The two specimens were obtained from the same patient on the sixth and seventh days of an illness that had been diagnosed as nonparalytic poliomyelitis. Paralysis developed in five days in all mice injected with inoculum from the two specimens. The Coxsackie virus isolated from this patient was designated as California 1. Neutralizing antibodies for the California 1 strain of Coxsackie virus could not be demonstrated in serum obtained from the patient early in the illness but were present in convalescent serum. Serum from the patient's daughter, who previously had had a similar illness, neutralized the strain of virus isolated from the father. In pathological examination of the skeletal muscles of mice infected with the California 1 virus, lesions typical of those produced by Coxsackie virus, group A, were noted. California 1 strain of the virus was not neutralized by immune serum prepared from several other strains of Coxsackie virus.

## Cancer Research, Chicago

12:615-690 (Sept.) 1952

Immunologic Aspects of Cancer: A Review. T. S. Hauschka.—p. 615.
Localization of Sulfapyrazine in Cancer Tissue Upon Glucose Injection. C. D. Stevens, M. A. Wagner, P. M. Quinlin and A. M. Kock.—p. 634.
Effects of Tumor Growth on Ascorbic Acid Concentration of Mouse Organs. E. M. Leise, E. K. Harvey and A. B. Schwanfelder.—p. 640.
Effects of Administration of Ascorbic Acid and of Rutin on Transplantability of Hepatoma and on Ascorbic Acid Levels of Mouse Organs. E. M. Leise, A. B. Schwanfelder and E. K. Harvey.—p. 643.
Effects of Dietary Riboflavin and Pantothenic Acid on Metabolism of 2-Aminofluorene. J. B. Allison and A. W. Wase.—p. 647.
Action of Cortisone and ACTH on Transplanted Mouse Tumors. R .G. Gottschalk and A. Grollman.—p. 651.
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Carcinogenicity of 1, 2-Benzanthracene. P. E. Steiner and J. H. Edgcomb. —p. 657.
Studies on Tissue Metabolism by Means of in Vivo Metabolic Blocking Technics. I. Survey of Changes Induced by Malonate in Tissues of Tumor-Bearing Rats. H. Busch and V. R. Potter.—p. 660.
Incorporation of Formate-$C^{14}$, Glycine-2-$C^{14}$, Adenine-4,6-$C^{14}$, and Phosphate-$P^{32}$ into Nucleic Acids. A. H. Payne, L. S. Kelly and H. B. Jones.—p. 666.
Effects of Atabrine and Certain Related Substances on Development of Liver Tumors Due to Azo Dyes. H. W. Rumsfeld, Jr., C. C. Clayton and C. A. Baumann.—p. 671.
Effects of A-Methopterin on Formate Incorporation into Nucleic Acids of Susceptible and Resistant Leukemic Cells. H. E. Skipper, L. L. Bennett Jr. and L. W. Law.—p. 677.
Effect of Irradiation on Lymphoid Tissue Nucleic Acids in C57BL Mice. P. P. Weymouth and H. S. Kaplan.—p. 680.

## Delaware State Medical Journal, Wilmington

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Key to Human Behavior. A. W. Gottschall.—p. 195.
Schizophrenic Reaction Following Course of ACTH Treatment. H. G. De Cherney.—p. 197.
Psychiatric Use of Isonicotinic Acid Hydrazide: A Case Report. J. A. Flaherty.—p. 198.
Some Aspects of In-Patient Psychiatric Treatment of Children. D. Johnston.—p. 200.
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Progress Made to Date in Fluoridation of Public Water Supplies. M. H. Jeffreys.—p. 242.
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Role of Speech Therapist in Cleft Palate Clinic. M. L. Gilmore.—p. 249.
Advantages to Orthodontist of Group Approach in Treatment of Cleft Palate Patient. L. Kreshtool.—p. 251.
Will the Child Outgrow His Speech Problem? D. Schantz-Hansen. —p. 252.
Understanding the Sick Child. A. Lammers and H. Cole.—p. 255.
Co-operation Between Public Health Personnel and School Nurses. M. M. Klaes.—p. 258.
Improvised Physical Therapy Equipment and Technique of Use in Home. C. Thomas and M. S. Garfinkel.—p. 259.

## Endocrinology, Springfield, Ill.

**50:**587-694 (June) 1952. **Partial Index**

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Production of Corticoids by Rat Adrenals in Vitro. M. Saffran, B. Grad and M. J. Bayliss.—p. 639.
Inhibition of Catabolic Effect of Adrenocorticotropic Hormone (ACTH) in Rats by Diet High in Potassium Chloride. J. E. Whitney and L. L. Bennett.—p. 657.
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**51:**1-74 (July) 1952. **Partial Index**

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Thyroid and Reproductive Performance in Adult Male Guinea Pig. W. C. Young, B. Rayner, R. R. Peterson and M. M. Brown.—p. 12.
Protective Effect of Steroids Against Acute Egg-White Toxicity in Adrenalectomized Rats. G. Chen and A. Wickel.—p. 21.
Effect of Testosterone on Muscle and Other Tissues and on Carcass Composition in Hypophysectomized, Thyroidectomized, and Gonadectomized Male Rats. R. O. Scow.—p. 42.
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Effect of Thyroidectomy on Mortality and Peripheral Blood Changes of Rat Subjected to Whole Body X-Irradiation. A. L. Kretchmar, H. J. Gomberg, D. E. Weyant and F. H. Bethell.—p. 59.
Effects of Adrenal Cortical Extract on Renal Function in Hypophysectomized Rats. W. R. Boss, C. M. Osborn and A. A. Renzi.—p 66.

## Hawaii Medical Journal, Honolulu

**12:**1-84 (Sept.-Oct.) 1952

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Cutaneous Manifestations of Internal Diseases. H. M. Johnson.—p. 26.
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## Illinois Medical Journal, Chicago

**102:**221-284 (Oct.) 1952

Diabetes Mellitus—Orientation. C. Striker.—p. 235.
Mortality and Prognosis in Small Bowel Resection. R. M. Mayer, I. F. Stein Jr. and K. A. Meyer.—p. 242.
Medicine and Freedom of Choice. E. E. Irons.—p. 246.
Organized Medicine and Its Service. H. M. Camp.—p. 251.
*Effects of Various Types of Analgesia and Anesthesia on the Newborn. C. M. Carey.—p. 256.
Recent Advances in Cardio-Vascular Medical Therapy. O. P. J. Falk. —p. 259.
Search for Foreign Bodies in Tissues. D. A. Willis.—p. 263.
New Technique for Topical Anesthesia of the Urethra. J. E. F. Laibe. —p. 266.

**Effects of Anesthesia During Labor on the Newborn.**—Carey reviewed the records of 1,784 deliveries made in one hospital from June to December, 1950, to ascertain the relationship of asphyxia neonatorum to premedication, anesthetic, and length of labor. Of the women delivered, 747 were primiparas. When no anesthesia was used during delivery the incidence of neonatal asphyxia was 2.88%. With nitrous oxide anesthesia the incidence was 3.85%; with ethylene it was 7.96%; with nitrous oxide and ethylene, 8.31%; with ethylene and ether, 30%; with ether, 33.33%; and with nitrous oxide, ethylene, and ether, 44.44%. Preanesthetic medication with meperidine (demerol®) hydrochloride, with or without scopolamine hydrobromide, resulted in an incidence of neonatal asphyxia of about 8%. With barbiturates or with morphine, meperidine, and scopolamine the incidence was 16.66%. With no premedication the incidence was 20.54%, but this was due to the fact that this group included patients in whom cesarean section was performed for placenta abruptio, placenta praevia, or failure to deliver during a test of labor, i. e., the type of labor, not the lack of premedication, was responsible. When the length of labor was less than 12 hours, the incidence of asphyxia was 9.27%; when it was over 24 hours, the incidence was 26.22%. The author stresses the need of individualization in the use of analgesics and anesthetics during labor.

## Industrial Medicine and Surgery, Chicago

**21:**461-508 (Oct.) 1952. **Partial Index**

Research on Chronic Toxic Effects from Long Exposure to Vapors of Pure Gasoline. A. Amorati, C. Cacciari and F. M. Troisi.—p. 466.
Value of Early Mobilization in Treatment of Fractures. P. A. Wade. —p. 469.
Skin Hazards in Railroad Roundhouses and Machine Shops. L. Schwartz. —p. 482.
Medullary Nailing in Treatment of Industrial Injuries. D. M. Street. —p. 485.
*Recovery from Anthrax Meningitis. D. Kindler.—p. 487.

**Recovery from Anthrax Meningitis.**—While anthrax is rare, it is common enough among wool workers that the physician should always be suspicious of cutaneous lesions in such workers. The incidence of meningeal involvement in anthrax is about 5%. Treatment for this complication should be instituted immediately if clinical evidence of meningeal irritation appears during infection. The author reports a patient who recovered from anthrax meningitis. He was given a total of 500 cc. of anti-anthrax serum intramuscularly: 100 cc. was given initially, and 50 cc. was given every eight hours thereafter for eight doses. He also received a total of 110,000 units of penicillin intrathecally: 30,000 units was given originally, followed by 20,000 units every 12 hours until five doses had been given. A total of 4,400,000 units of penicillin was given intramuscularly in doses of 100,000 units every three hours for four days, followed by 50,000 units every three hours for three days. Wet penicillin dressings were applied to the cutaneous lesion. Sulfadiazine was administered in a total dose of 28 gm., 4 gm. being given initially followed by 1 gm. every four hours for four days.

## Journal of Experimental Medicine, New York

**96:**281-400 (Oct.) 1952

Intrarenal Pressure During Experimental Renal Hypertension. H. G. Swann, J. M. Prine, V. Moore and R. D. Rice.—p. 281.
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Half-Life of Homologous Gamma Globulin (Antibody) in Several Species. F. J. Dixon, D. W. Talmage, P. H. Maurer and M. Deichmiller. —p. 313.
Studies on a Proteolytic Enzyme in Human Plasma. VIII. Effect of Calcium and Strontium Ions on Activation of Plasma Proteolytic Enzyme. O. D. Ratnoff.—p. 319.
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Id.: II. Description of Growth Curve and Its Relation to Cytopathogenicity of Poliomyelitis Virus. W. F. Scherer and J. T. Syverton. —p. 369.
Id.: III. Propagation of Poliomyelitis Viruses in Tissue Cultures Devoid of Nerve Cells. W. F. Scherer and J. T. Syverton.—p. 389.

## Journal of Gerontology, St. Louis

**7:**351-532 (July) 1952. **Partial Index**

Metabolic and Hematologic Effects of Chronic Administration of ACTH to Young and Old Men. L. E. Duncan Jr., D. H. Solomon, E. K. Rosenberg and others.—p. 351.
Effects of Administration of Testosterone Propionate on Testicles in Senescent Male. J. J. Cordonnier.—p. 375.
Aging in Apparently Normal Men. IV. Roentgenologic Appearance of Thorax and Thoracic Organs. W. S. Tirman and J. B. Hamilton. —p. 384.
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Treatment of Parkinson's Syndrome with Tropine Benzohydryl Ether Methane Sulfonate and Other Drugs. G. M. Tanaka and J. C. Edwards.—p. 405.
Jobs for Older Workers. S. Barkin.—p. 426.
Note on Meaning of Aging. A. R. Chandler.—p. 437.

## Journal of International College of Surgeons, Chicago

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## Journal of Investigative Dermatology, Baltimore

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## Journal of Neurosurgery, Springfield, Ill.

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Phantom Limb in Paraplegic Patients: Report of Two Cases and Analysis of Its Mechanism. A. W. Cook and W. H. Druckemiller.—p. 508.
Ocular Complications of Carotid Angiography; Ocular Signs of Thrombosis of Internal Carotid Artery. F. B. Walsh and G. W. Smith. —p. 517.
Our Training Programs and the Future of Neurological Surgery. P. C. Bucy.—p. 538.

**Localization of Intracranial Lesions by Radioactive Isotopes.**—Peyton and associates had previously used fluorescein sodium in diagnosis of brain tumors by differential fluorescence. In this report they describe their experiences with radioactive diiodofluorescein (DIF) and more recently with radioactive iodinated human serum albumin (RIHSA), which remains longer in the blood stream, so that suspicious areas can be examined again 24 or even 48 hours later without injection of additional radioactive solution. Various types of Geiger-Müller counters have been used as well as a scintillation counter. The authors plan to try out a multiple counter consisting of a bank of 18 tubes arranged so they will survey both sides of the head simultaneously. Cases are described, and radioactive counting is explained with the aid of diagrams. The authors conclude that about 70% of intracranial tumors can be correctly localized with radioactive isotope examination alone, but, if the clinical data are also utilized, correct localization can be obtained for up to 94%. There are biological limitations to this method that lead to erroneous diagnoses unless the clinical data are utilized. Cystic and necrotic lesions do not take up the radioactive isotope and therefore may give a false localization with low counts over the lesion. Small lesions do not take up enough of the dye to give a good differential count, and some tumors, especially oligodendrogliomas, take up little of the isotope. Midline lesions, which are often small, and posterior fossa lesions are difficult to localize. Lesions other than tumors that lower the blood-brain barrier, such as vascular lesions and, possibly, inflammatory and demyelinizing lesions, give a focus of high counts. Thus this procedure does not differentiate neoplastic and nonneoplastic lesions. The lesions most easily localized with isotope encephalometry are large lesions in the cerebral hemisphere associated with edema. Glioblastoma, meningioma, and metastatic tumors give the best differential counts.

## Journal of Nutrition, Philadelphia

48:1-124 (Sept.) 1952

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Influence of Dietary Fat and Carbohydrate on Reproduction and Lactation in Rats. C. E. French, R. H. Ingram, L. K. Knoebel and R. W. Swift.—p. 91.

## Journal of Pediatrics, St. Louis

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Constitutional True Sexual Precocity. S. H. Walker.—p. 251.
Mucolytic Enzyme Systems. XVIII. Nonspecific Hyaluronidase Inhibitor Concentrations in Blood Serum of Siblings and Parents of Children with Rheumatic Fever. F. H. Adams, D. Glick, R. C. Anderson and P. Dwan.—p. 258.
Electroencephalographic Diagnosis of Cerebral Pathology in Infants During Sleep. I. Rationale, Technique, and Characteristics of Normal Sleep in Infants. P. Kellaway and B. J. Fox.—p. 262.
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Optimum Dose of Pollen in Treatment of Pollinosis of Children. S. J. Levin.—p. 294.
Reduction of Mortality in Premature Nursery. II. Incidence and Causes of Prematurity: Ethnic, Socioeconomic and Obstetric Factors. H. Bloch, H. Lippsett, B. Redner and D. Hirschl.—p. 300.
Further Studies in Congenital Cranial Osteoporosis (Craniotabes). II. Its Relationship to Cranial Molding and Duration of Labor. E. Boder. —p. 305.
Diagnosis and Management of Congenital Hypertrophic Pyloric Stenosis. H. F. Rheinlander and O. Swenson.—p. 314.
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Acute Gangrenous Appendicitis in a Premature Infant. J. F. Meyer. —p. 343.

## Journal of Thoracic Surgery, St. Louis

**24:**325-434 (Oct.) 1952

Traumatic Saccular Aneurysm of Thoracic Aorta. R. K. Hollingsworth, W. W. Johnston and J. F. McCooey.—p. 325.
*Healing of Extensive Cardiac Wounds. C. G. Thomas Jr. and S. E. Ziffren.—p. 346.
Hemopericardium and Constrictive Pericarditis. J. L. Ehrenhaft and R. E. Taber.—p. 355.
*Rupture of Esophagus. R. L. Anderson.—p. 369.
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Surgical Management of Pulmonary Emphysema. G. L. Crenshaw and D. F. Rowles.—p. 398.
Obstructive Pneumonitis Secondary to Bronchial Adenoma. R. P. McBurney, O. T. Clagett and J. R. McDonald.—p. 411.
Adenocarcinoma Developing in Peripheral Bronchial Adenoma: Report of Case. W. Umiker and C. F. Storey.—p. 420.
Induced Pulmonary Tumors. W. J. Burdette.—p. 427.

**Healing of Extensive Cardiac Wounds.**—Experiments were made on two groups of dogs to study the healing of the myocardium following extensive incisional and excisional wounds of the anterior wall of the left ventricle. In the first group, an area measuring about 3 by 4 cm., including the entire thickness of the left ventricular wall, was excised. The resulting defect in the ventricular wall was closed by interrupted through-and-through silk sutures. Fifteen dogs were available for periodic examinations during the course of wound healing, with observations made over 46 months. In the second group, a linear incision about 4 cm. long was made in the left ventricular wall parallel to the interventricular septum beyond the gross arborizations of the rami of the anterior descending branch of the left coronary artery. Closure was effected as described in the first group. Twelve dogs were observed over a period of 11 months. Serial electrocardiograms, which were procured during all phases of the procedure, as well as early and late in the postoperative period, revealed mild changes in the T waves, similar to those observed by Fowler and associates. The animals were killed at periodic intervals under pentobarbital sodium anesthesia. In each instance, the heart was observed directly for evidence of cardiac aneurysm. Results showed that repair of the large cardiac wounds was characterized by production of a dense scar uniting the wound margins, apparently without impairing cardiac function. This scar was half as thick as the adjacent normal ventricular wall and attenuation usually continued until the scar was 30% as thick as the ventricular wall after several months. There was considerable variation in the breadth of the scar. No evidence of aneurysm was observed in the scars under normal and under increased cardiac load. Embolism was not observed following any of the procedures. The strongest scar was obtained with the shortest incision through the thickest part of the myocardium in conjunction with maximum wound apposition by sutures causing minimal ischemia. Wound dehiscence seemed to depend primarily on the amount of necrosis of cardiac muscle caused by the wound closure. With experience in the placement of sutures and the attainment of appropriate degrees of tension, this complication should be avoided.

**Rupture of Esophagus.**—Rupture of the esophagus is reported in four men between the ages of 48 and 59 years, who had the typical history and physical indications associated with spontaneous rupture of the esophagus. It is suggested that the term "spontaneous" is a misnomer in most cases because the rupture is usually associated with disease of or change in the esophageal wall. In two of the author's patients the disease of the esophagus was symptomatic, while in the other two there was history of peptic ulcer, which is often associated with esophagitis. In three of the patients there was definite history of an inadequate diet and alcoholism. All four had disturbance of protein metabolism, with a low total serum protein level and a reversal of the albumin-globulin ratio. All these factors contributed to weakness of the esophageal wall. The sudden occurrence of severe epigastric pain was preceded by vomiting in only one patient, but in the other three it was preceded by a large meal or an alcoholic bout. These conditions probably contributed to increased intraluminal pressure in the esophagus. Increase in intraluminal pressure and further weakening of the esophageal wall were responsible for the rupture in all cases. In none of the patients was definitive surgical intervention carried out at the proper time. Immediate thoracotomy, with closure of the perforation and reestablishment of normal structure and function, is the treatment of choice. The delay in carrying out thoracotomy and repair contributed to postoperative complications and prolonged convalescence in the author's patients. All survived despite delayed treatment, illustrating that, if the patient survives for 48 hours, treatment may be more conservative, and the patient has a reasonable chance of surviving. With early diagnosis, which is not too difficult considering the diagnostic triad of rapid respiration, abdominal rigidity, and subcutaneous emphysema, and with early treatment the prognosis is good. Most diagnostic failures are due to lack of knowledge or failure to consider the possibility of rupture of the esophagus.

## Medical Annals of District of Columbia, Washington

**21:**471-530 (Sept.) 1952

Inhalational Therapy. P. F. Jaquet.—p. 471.
Use and Abuse of Some New Drugs. E. W. Kailin and J. C. Sullivan. —p. 478.
Electrocardiographic Manifestations of Coronary Artery Heart Disease. J. M. Barker.—p. 483.
Marital Conflict and Functional Illness. S. A. Steiner.—p. 486.
Resolution of Paranoid Psychosis. L. Salzman.—p. 489.

## Medicine, Baltimore

**31:**221-329 (Sept.) 1952

Late Effects of Internally-Deposited Radioactive Materials in Man. J. C. Aub, R. D. Evans, L. H. Hempelmann and H. S. Martland.—p. 221.

## Missouri State Medical Assn. Journal, St. Louis

**49:**733-796 (Sept.) 1952

Gallbladder Problem. R. L. Sanders.—p. 733.
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## New England Journal of Medicine, Boston

**247:**455-498 (Sept. 25) 1952

*Surgical Closure of Defects of Interauricular Septum by Use of Atrial Well. R. E. Gross, A. A. Pomeranz, E. Watkins, Jr. and E. I. Goldsmith.—p. 455.
Evaluation of Pilot Clinics: Mass Screening or Health-Protection Program. V. A. Getting and H. L. Lombard.—p. 460.
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Medicine + Industry = Occupational Health. J. F. McCahan.—p. 470.
Occupational Medicine. H. L. Hardy.—p. 473.

**247:**499-540 (Oct. 2) 1952

Intussusception: Review of Experience at Massachusetts General Hospital, 1937-1951. G. H. Lawrence and H. Ulfelder.—p. 499.
Murmur of Peripheral Arteriovenous Fistula. E. A. Edwards and H. D. Levine.—p. 502.
Malignant Neoplastic Disease Discovered in Chest X-Ray Surveys. G. Bondi and V. Leites.—p. 506.
Trichinosis with Neurologic and Mental Manifestations. R. A. Scott, R. E. Johnson and D. Holzman.—p. 512.
Medical Progress: Occupational Medicine. H. L. Hardy.—p. 515.

**Closure of Septal Defects.**—In experiments on dogs a method was developed whereby moderate or large size defects of the interauricular septum can be closed surgically. A rubber bag or well, open at both ends, is attached to an auricular wall, and the incision into the auricle is made through the bottom of this attached sac. Blood rises up into such a well to a height equal to the intra-auricular pressure. Through the pool of blood, kept fluid by heparin, it is possible to pass one or several fingers into the auricle to explore it, to locate accurately any septal defect, and to close it. After extensive trials with the use of auricular

"wells" in dogs, closure of defects of the interauricular septum was attempted in six children between the ages of 4 and 16. In none of these patients was there the slightest difficulty in attaching the rubber well to the enlarged right auricle. Three methods of attempting septal closure were employed. Screw-on plastic buttons of the Hufnagel type were used in the first three patients, all of whom died within a few days. In each of these three patients the button worked loose because there was an incomplete rim of septal tissue around the opening and hence not sufficient substance to hold the buttons in place securely. In the fourth patient a large high septal defect was closed with a sheet of polyethylene 0.5 mm. thick. It covered the septal defect quite well but projected down unnecessarily over the annulus of the tricuspid valve. The patient died suddenly on the third postoperative day, and necropsy revealed that a clot under the excess plastic had extended down and obstructed the tricuspid valve orifice. In the fifth patient, a large septal defect was closed successfully with a piece of nylon, accurately cut and shaped and carefully sutured into place. The patient was in excellent condition two months after operation, and the cardiac murmur had disappeared. In the sixth patient, two smaller septal openings were closed by direct stitching and approximation of the septal margins. The patient made a rapid recovery and was in excellent condition two months later; the precordial murmur had disappeared.

## New Jersey Medical Society Journal, Trenton

**49:**415-450 (Oct.) 1952


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Role of the General Practitioner in Modern Psychiatry. C. N. Baganz. —p. 432.
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## New York State Journal of Medicine, New York

**52:**1938-2058 (Aug. 15) 1952

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The Failing Lung. W. S. McCann, F. W. Lovejoy Jr. and P. N. G. Yu. —p. 1983.
Undetected Seedbed in Tuberculosis. E. M. Medlar.—p. 1987.
Thoracic Surgery After Age of 50. W. Woodruff.—p. 1990.
Pulmonary Thromboembolism: Diagnosis and Treatment. I. S. Wright and W. T. Foley.—p. 1994.
Treatment of Pulmonary Tuberculosis at Home. L. Schneider.—p. 1999.
Present Trends in Treatment of Pneumonias. P. A. Bunn.—p. 2005.
Alveolar Cell Lung Cancer. W. L. Watson.—p. 2010.
Pentaerythritol Tetranitrate: New Drug for Treatment of Coronary Insufficiency. M. Plotz.—p. 2012.
Failure of Hyaluronidase to Increase Rate of Absorption of Depot Insulin. C. Weller and W. Liccione.—p. 2015.
Sedation Without Side-Effects by Use of Niacin Hydrobromide. T. M. Feinblatt and E. A. Ferguson Jr.—p. 2017.
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**52:**2063-2174 (Sept. 1) 1952

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Sporotrichosis: Etiologic Considerations and Report of Additional Cases from New York. J. I. Singer and J. E. Muncie.—p. 2147.
Analysis of Needs for Cerebral Palsied in Representative Suburban County and Plan for Their Management. R. V. Martin.—p. 2154.
Flicker Photometry and Electrocardiography: Correlation. L. H. Golden and E. M. Cordasco.—p. 2157.


## Ohio State Medical Journal, Columbus

**48:**793-888 (Sept.) 1952


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## Pediatrics, Springfield, Ill.

**10:**243-380 (Sept.) 1952


Prolonged Obstructive Jaundice in Infancy; General Survey of 156 Cases. D. Yi-Yung Hsia, P. Patterson, F. H. Allen Jr. and others.—p. 243.
*Intestinal Obstruction in Newborn Infant Due to Agenesis of Myenteric Plexus (Congenital Megacolon). W. J. Potts, J. D. Boggs and H. White. —p. 253.
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Respiratory Patterns in Newborn Infants as Determined by Airflow and Pneumographic Studies and Their Possible Relationship to Deficient Vagal Mechanism. H. C. Miller and F. C. Behrle.—p. 272.
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*Studies in Pancreatic Fibrosis; Cor Pulmonale: Clinical and Pathologic Observations. A. S. Nadas, G. Cogan, B. H. Landing and H. Shwachman.—p. 319.
Studies of Immunology of Newborn Infant; Interference with Active Immunization by Passive Transplacental Circulating Antibody. J. J. Osborn, J. Dancis and J. F. Julia.—p. 328.


**Intestinal Obstruction in Newborn Infant.**—A report is presented of 10 newborn infants who were hospitalized with symptoms of acute intestinal obstruction, but who were proved to have functional obstruction due to agenesis of the myenteric plexus of various portions of the colon (congenital megacolon). Vomiting, constipation, and abdominal distention during the first few days of life were the presenting symptoms in all cases. All had the classical roentgenographic picture of obstruction of the bowel. One of the 10 patients, who had previously had an exploratory operation elsewhere, had peritonitis on admission and died the following day at 3 weeks of age. At surgical exploration in a 3-day-old patient no mechanical obstruction was found and the abdomen was closed. Medical treatment was given, but the patient died at 1 month of age. In seven patients exploration of the abdomen was performed, and a transverse colostomy done at the time or at a later date. Two of these patients were moribund and died the day after colostomy was performed. Another lived for two months after transverse colostomy and died of malnutrition, infection, and dehydration. At necropsy the entire colon from the cecum to the rectum contained no ganglions. The fourth patient died of unrecognized and misinterpreted small bowel obstruction two weeks after colostomy. Three patients survived transverse colostomy but had stormy courses requiring hospitalization for two, five, and five months respectively. The 10th patient had classical symptoms of neurogenic bowel obstruction for the first three days of life. For no reason at all the bowels began to move normally and continued to do so for five weeks. Then constipation again became severe, and the patient proved to have a typical case of congenital megacolon. Because dilatation was limited to the upper rectosigmoid, resection of the isolated dilated segment and end-to-end anastomosis were performed. The patient did well for about six months, when all the previous symptoms returned. This time the long spastic distal segment of bowel was removed and after the splenic flexure was freed, the descending colon was brought down to and anastomosed with the rectal stump. The infant remained well a year after the operation, with normal bowel evacuations. Agenesis of the myenteric plexus often manifests itself by intestinal obstruction in the newborn infant. Medical management in such cases is not effective. If the infant's condition warrants,

immediate resection of the neurogenically abnormal bowel should be done. In the poor risk infant sigmoid-colostomy is the procedure of choice. After the infant has recovered and is gaining weight normally, a suitable time may be chosen for the definitive operation of rectocolostomy.

**Cor Pulmonale in Pancreatic Fibrosis.**—Of 150 children with pancreatic fibrosis, 46 had severe pulmonary disease as demonstrated by physical examination and roentgenogram, with limitation of activities. Eight of the 46 had cor pulmonale. One of these eight died in right heart failure, but the others showed only electrocardiographic changes characteristic of right ventricular hypertrophy. The postmortem findings in 35 children who had died of pancreatic fibrosis were compared with those of a control group of children of same age range who died during the same period but did not have chronic pulmonary disease, renal disease, anemia, or primary and secondary heart disease. There were no diagnostic differences between the two groups in cardiac weight or absolute right ventricular thickness. The ratio of right to left ventricular thickness, however, was higher in the group with pancreatic fibrosis, as was the ratio of cardiac weight to body weight. Only 2 of the 35 necropsies revealed visceral edema and significant congestion that was suggestive of frank right ventricular failure. Physiological and pathological considerations are presented concerning the development of pure pulmonary hypertension and its relationship to cor pulmonale, compensated or decompensated. The authors' data suggest that the pulmonary involvement associated with infection is still the principal threat to life in patients with pancreatic fibrosis and the one toward which major therapeutic efforts should be directed.

## Proc. Soc. Exper. Biol. & Med., Utica, N. Y.

**80:**565-786 (Aug.-Sept.) 1952. **Partial Index**


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Immunization of Mice with Inactivated Type 2 Poliomyelitis Virus Against Types 2 and 3 Viruses. J. Casals, P. K. Olitsky and L. V. Brown.—p. 731.
Morning Changes in Number of Circulating Eosinophils in Infants. F. Halberg and R. A. Ulstrom.—p. 747.


**Isolation of Mycobacterium Tuberculosis in Embryo Yolk Sac.**—Previous investigators demonstrated that when pure cultures of Mycobacterium tuberculosis are inoculated into the yolk sac of embryonated eggs, they proliferate with great rapidity. Brueck and Buddingh decided to investigate whether this method could be used for the rapid isolation of Myco. tuberculosis from materials collected from patients. A total of 50 specimens of various types were subjected to yolk sac inoculation in eggs embryonated for five to eight days. Thirty-nine of these 50 were derived from patients with various types of tuberculous infection and 11 were obtained from negative controls. Acid-fast bacilli were demonstrable within four to six days after inoculation in every instance in which positive results were obtained. In each of these cases the acid-fast bacilli demonstrated in the yolk sac cultures proved to be Myco. tuberculosis by guinea pig inoculation. Acid-fast bacilli were not demonstrated in yolk sacs inoculated with materials from the negative controls. The yolk sac of the developing chick embryo apparently provides exceptionally favorable nutritional and environmental conditions for the rapid proliferation of Myco. tuberculosis. By this means the period for detecting Myco. tuberculosis is shortened considerably compared to that required in the established cultural methods and by animal inoculation. The method has been found to be especially valuable in establishing the diagnosis in cases of tuberculous meningitis and tuberculous pericardial, pleural, and peritoneal effusions. Limited experience thus far indicates its usefulness in evaluating the effect of therapy in cases of tuberculous meningitis.

## Public Health Reports, Washington, D. C.

**67:**929-1068 (Oct.) 1952. **Partial Index**


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## South Dakota J. Med. & Pharmacy, Sioux Falls

**5:**243-272 (Sept.) 1952


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Your Medical School. W. L. Hard.—p. 249.
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## Southern Medical Journal, Birmingham, Ala.

**45:**885-1014 (Oct.) 1952


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Pelvic Abscess. C. G. Johnson, C. C. Collins and H. B. Webster Jr.—p. 926.
Relief of Pain by Transorbital Leukotomy. C. E. Patterson and C. C. Nash.—p. 934.
Intracerebral Hematomas: Survey of 106 Verified Cases. G. L. Odom, B. M. Bloor and B. Woodhall.—p. 936.
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Considerations of Cardiac Hypertrophy in Sickle Cell Anemia. V. A. Stembridge and R. H. Rigdon.—p. 948.
*Prevention of Erythroblastosis Fetalis by Use of Rh Hapten. A. L. Dippel.—p. 954.
Problem of Sensitization from Topical Therapeutic Agents. S. Prystowsky.—p. 960.
Evaluation of Available Therapeutic Agents in Ophthalmology. J. B. Rogers.—p. 964.
Polycythemia Secondary to Brain Tumor: Report of Two Cases. C. R. Holmes, F. E. Kredel and C. B. Hanna.—p. 967.
Role of General Practitioner in Community Medical Service. J. P. Sanders.—p. 972.


**Cortisone and Corticotropin as Therapeutic Agents.**—Stone and Spies present clinical summaries of 15 patients arbitrarily selected from about 200 who were treated with corticotropin or cortisone for uncomplicated rheumatoid arthritis and for arthritis associated with iritis or psoriasis. The effect immediately following treatment was similar in all the conditions treated. The symptoms of inflammation in the joints, skin, eyes, nervous system, or lymph nodes rapidly cleared. In one case, symptoms arising from serum reaction were suppressed by corticotropin. In chronic arthritis the effects of corticotropin and cortisone are difficult to assess. Remissions occurred in about one-sixth of the patients, but the authors consider this consistent with the natural course of the disease. Corticotropin and cortisone have no effect on permanently altered structure, but in selected cases these hormones give symptomatic relief and increase functional capacity so that resumption of useful activity is possible. Certain

lesions arising in the skin and eyes respond to the local application of cortisone ointment. Corticotropin and cortisone alone are not sufficient; coexisting disorders, especially nutritional deficiency, should receive proper treatment. The authors object to the application of the term "side-effects" to what are the real effects of these hormones when they are given in excessive doses. Overdosage should be avoided, even if it means that the patient cannot be given the amount of hormone necessary to relieve his symptoms completely. In every patient, the cause of the disorder should be sought, since corticotropin and cortisone effect only symptomatic relief. Response to these hormones varies from patient to patient so that it is impossible to set definite or minimum doses.

**Regression of Cervical Carcinoma in Situ Following Use of Aureomycin.**—Epidermoid cancer of the cervix arises from the tissue of the squamocolumnar junction. Carcinoma in situ is believed to be the preinvasive stage of this malignant growth. Before cytological staining was practiced, carcinoma in situ was considered rare, but routine cervical smears reveal an incidence of 1% in well women in industry and of 3% in women complaining of pelvic inflammatory disease or menorrhagia. Serial cell studies revealed that it may not progress further for up to 6 years; however, invasion ultimately follows in most cases. There being indications that cervical cancer developed in a chronic infectious inflammatory bed, it was decided to study the effects of antibiotics, chemotherapy, and hormones on cervical cells and the embryo neoplasm. No regression was observed with use of the sulfonamides, penicillin, or streptomycin, but in 8 of 19 cases apparent regression followed aureomycin therapy, with three recurrences within 6 months after cessation of treatment. Aureomycin hydrochloride was given as a 250 mg. vaginal suppository each evening at bedtime. Case reports are given of one patient who responded and one who did not. The author does not assert that aureomycin is a cure for cancer, because none of the invasive lesions responded by regression. Some in situ cancers and lymphogranuloma venereum seem to have common etiological factors. In answer to whether the regression is brought on by an antivirus or an anticarcinogenic action, the author says that some investigators observed an anticarcinogenic effect of aureomycin on tissue cultures. The author concludes tentatively that in situ cancer is a neoplastic infectious process that is not yet wholly autonomous. This does not mean that it will not become malignant in future years if it remains untreated.

**Rh Hapten in Prevention of Erythroblastosis Fetalis.**—Various drugs, hormones, and blood plasma have been tried with little success in the prophylaxis of erythroblastosis fetalis. Recently Carter produced an Rh hapten with which she has obtained encouraging results. Goldsmith obtained even more promising results after she modified Carter's technique. Adhering largely to Goldsmith's technique Dippel extracted Rh hapten with water, alcohol, and ether from outdated Rh positive blood obtained from the blood banks of hospitals. The product is a cholesterol-like lipid with little or no antigenic properties. It is white to light brown and is soluble in ether or high concentrations of alcohol. The yield is low, amounting to only 400 to 500 mg. per pint of whole blood. This comprises an average dose. It is put up in vials containing 2 cc. of dehydrated alcohol and is administered intramuscularly in the gluteal area. The contents of the vial are drawn into a sterile syringe, after which an equal amount of 2% procaine hydrochloride is added to reduce tissue discomfort, and the solutions are mixed. A flocculated solution results, but, when injected, it rarely produces local irritation, and never a general reaction. Size of the dose and frequency of administration have been dictated by the response shown in antibody titer. Currently, doses of 400 mg. are given weekly, and titers are obtained simultaneously. Dippel describes several cases that reveal some of the difficulties encountered in this treatment. Since in most of the early cases he had not been able to completely neutralize the Rh antibody titer, he attempted to do so by rapidly administering hapten as soon as a patient with a positive titer came under observation. Patients were hospitalized for 48 hours and given an injection of hapten every four hours for a total of 12 injections. Furthermore, patients previously isoimmunized were not included in the current series unless seen during the first trimester of pregnancy. Therapy is begun as soon as a presumptive diagnosis of pregnancy can be made. A case is described in which the successful outcome of the pregnancy is credited to this form of Rh hapten therapy.

## Southwestern Medicine, El Paso, Texas

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General Principles of Dermatological Therapy. G. K. Rogers.—p. 323.
Current Status of Plasma Volume Expanders. J. E. Rhoads.—p. 326.
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## Surgery, St. Louis

32:443-604 (Sept.) 1952. **Partial Index**

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Comments on Halsted's Contributions to Arterial Surgery with Particular Reference to Progressive Occlusion of Large Arteries by Means of Aluminum Band. E. Goetsch.—p. 488.
Impact of Halsted Upon Surgical Technique of Today with Particular Reference to His Operation for Hernia. W. F. Rienhoff Jr.—p. 493.
The Story of Harvey Cushing's Appendix. S. C. Harvey.—p. 501.
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Fruition of Halsted's Concept of Surgical Training. B. N. Carter.—p. 518.
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## Tennessee State Medical Assn. Journal, Nashville

45:381-422 (Oct.) 1952

Surgery in Diverticulitis: Review of Surgically Treated Cases at Vanderbilt and St. Thomas Hospitals Within Recent Years. J. L. Herrington Jr.—p. 381.
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## U. S. Armed Forces Med. J., Washington, D. C.

3:1241-1410 (Sept.) 1952

*New Local Treatment of Burns. D. S. J. Choy and W. E. Wendt.—p. 1241.
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Sedimentation Rate in Acute Cholecystitis. T. H. Hewlett.—p. 1267.
Some Practical Clinical Aspects of Leprosy. J. A. C. Gray.—p. 1297.
Gait Training for Above-the-Knee Amputee. H. M. Mendler, J. A. Shafer and R. C. Psaki.—p. 1329.
*Air Transportation of Acute Poliomyelitic Patients. H. C. Hunley Jr.—p. 1337.
Treatment of Malaria with Cortisone. O. A. Wurl, J. O. Gillespie and W. R. Beisel.—p. 1347.
*Fatal Lead Poisoning Simulating Poliomyelitis. A. F. Braff, D. O. Lynn and O. A. Wurl.—p. 1353.
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Right Lower Quadrant Pain. P. M. Burke.—p. 1367.
Sensitivity to Ointments Containing Wool Fat. H. K. Schwarzfeld.—p. 1371.
Tetanus Treated with Cortisone. L. C. Scheinberg.—p. 1377.

**New Local Treatment of Burns.**—Burn therapy techniques need revision in view of the demands of atomic warfare. It was thought that a nontoxic, biologically and chemically inert, adhesive, elastic, transparent, rapidly drying, film-forming, and peelable plastic, dispensed from an aerosol bomb or spray gun, would overcome most of the difficulties of standard burn dressings. Of a number of plastics tested in the laboratory, a modified polyvinyl chloride acetate copolymer in ethyl acetate solvent was selected for evaluation. In preliminary studies "gloves" of transparent plastic film were applied to the (unburned) digits and hands of several subjects by immersion or spraying. These preliminary tests proved impermeability for bacteria, adhesiveness to skin, elasticity, water resistance, flexibility and permeability to water vapor. The sprayable polyvinyl plastic was then tried on dogs in which about 20% of the body surface had been burned. The plastic dressing was sprayed on the burned area within 10 minutes of the burning. The ethyl acetate solvent evaporated within from 15 to 20 seconds, leaving a tough elastic, transparent plastic film adhering to the burned areas and the

surrounding, healthy skin. The open-air method was employed in the control animals. No statistically valid conclusions can be derived from the small series treated, especially with reference to relative healing times of the control and treated groups, but the results are encouraging. It is understood that adequate systemic therapy with fluid and electrolyte replacement, antibiotics, analgesics, and tetanus antitoxin, take precedence over any form of local therapy.

**Air Transportation of Patients with Acute Poliomyelitis.**—Recent studies have indicated that transportation over long distances may be harmful to a patient in the acute stage of poliomyelitis. Study of a series of 12 poliomyelitis patients transported by the Military Air Transport Service in 1950 supports this finding. Transportation by air involves preflight movement from hospital to airport and from airport to hospital after flight. While it has not been shown that the air-borne portion of the aerial journey adversely influences the outcome of bulbar involvement in poliomyelitis, the advisability of transporting such patients in the acute stage is questionable. Furthermore, the need for transporting a patient in the acute stage of poliomyelitis is questionable. The clinical management of poliomyelitis resolves itself into supportive and protective measures during the acute stages. If, during the acute stage, special lifesaving means are needed but not available locally, they could as easily be transported to the patient as vice versa.

**Fatal Lead Poisoning Simulating Poliomyelitis.**—In the case reported fatal lead poisoning was confused with bulbospinal poliomyelitis. The patient was a man, aged 23, who had been on duty with the Navy for four months and had been ill for three weeks. He now had progressive paralysis involving all extremities and a marked pain in his back and the muscles of his thighs. Twenty-four hours prior to admission he had had difficulty in swallowing and dyspnea. He was placed in a respirator, but died two days later. Chemical analysis of the blood post mortem revealed a lead content of 0.5176 mg. per 100 cc. Microscopic sections of the brain and spinal cord indicated a toxic type of encephalomyelopathy rather than an infectious process. The patient had been employed as a welder and pipe fitter for about four months. He had worked on galvanized and sheet metals and had, therefore, been exposed to the fumes of lead, zinc, and arsenic. During his 4 months in this occupation he had had a poor appetite and his intake of food had been small. No fresh milk had been available. Prior to recall to active duty, he had done electrical work, the exact nature of which was unknown. The diagnosis of lead poisoning predominantly affecting the nervous system depends on a high index of suspicion and a history of exposure to lead. The demonstration of abnormal concentrations of lead in the blood or urine is proof of the absorption of excessive quantities into the body.

### 3:1411-1580 (Oct.) 1952

Restoration of the Jaw. B. N. Soderberg, H. B. Jennings Jr. and J. E. McNelly.—p. 1423.
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Viral Hepatitis in U. S. Troops in Germany. J. R. Paul and D. M. Horstmann.—p. 1457.
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*Personality Changes Following Cardiac Arrest. J. N. Gordon, I. R. Sternlicht and O. M. Weaver.—p. 1469.
Oxypolygelatin as Plasma Substitute. J. S. Chen, M. L. Chen, S. S. Lin and A. S. Chang.—p. 1479.
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Paroxysmal Cold Hemoglobinuria. B. D. Hall.—p. 1519.
Infected Urachal Cyst. E. L. Lewis and J. C. Kimbrough.—p. 1525.
Onlay Tantalum Mesh: Emergency Replacement of Abdominal Wall Defect. D. D. Greene, S. J. Thomas Jr. and J. M. Thompson.—p. 1529.
Traumatic Diaphragmatic Hernia. D. E. Thomas.—p. 1535.
Acute Hemolytic Anemia with Infectious Mononucleosis. A. C. Mermann.—p. 1551.

**Personality Changes Following Cardiac Arrest.**—The case described by Gordon and his associates confirms the fact that personality changes may occur as a result of cerebral anoxia, especially when the anoxia is of sufficient duration to cause irreversible brain damage. The patient was a 21-year-old soldier who had a tonsillectomy. His throat was sprayed with 10% cocaine, and local procaine hydrochloride infiltration anesthesia was used. He was given 100 mg. of pentobarbital preoperatively. Shortly after the operation he went into a convulsive state, breathed deeply at the rate of four or five times a minute, and became cyanotic. He was immediately given oxygen by inhalation, and was intubated. A thoracotomy was performed about five minutes after the episode started. The heart was in complete arrest, and massage was started. One cubic centimeter of 1:1,000 epinephrine was injected into the heart muscle and, after about 10 minutes of massage, fibrillary vermicular movements were noted; 5 cc. of 2% procaine hydrochloride was injected intracardially, and massage was continued. Ten minutes later, irregular ventricular contractions were noted, and 10 cc. of 2% procaine was injected while massage was continued. In about five more minutes a regular beat was maintained and the chest was closed. Oxygen administration was continued by means of an endotracheal tube. Consciousness gradually returned, but the patient was still stuporous and could not swallow. The trachea was kept clear by suction. Several days later gastrostomy and tracheotomy were performed, On the following day the patient was able to void spontaneously but still did not respond to questioning. Several days later, oxygen therapy was discontinued, the tracheotomy tube was removed, and the patient was able to drink a cup of milk. Later the tracheotomy wound was closed, and the gastrostomy tube was removed. The patient began to talk, but was disoriented. Several days later he was removed to a neuropsychiatric ward, where he showed general mental retardation but was compliant to repeated urgings. He responded at a moronic level. Several months later he showed minimal improvement. His mother thought he was functioning at about 40% of his normal level but that most of his difficulty was in visual and memory areas. She noticed much improvement, since at first he had not recognized either her or his sister. The prognosis for further improvement under a concentrated retraining program appears to be good.

## Virginia Medical Monthly, Richmond

### 79:481-536 (Sept.) 1952

Indications for Tonsillectomy and Adenoidectomy in Children. G. S. Fitz-Hugh.—p. 483.
Salicylate Intoxication. J. A. Tobin and G. R. Hennigar.—p. 486.
Nonoperative Treatment of Perforated Peptic Ulcer: Report of 20 Cases. H. U. Stephenson Jr.—p. 488.
Treatment of Bronchial Asthma with New Natural Steroid Complex. M. Millman and G. E. Maggio.—p. 494.
Chronic Infectious Granuloma of Large Bowel: Case Report. H. H. Galston.—p. 500.

## West Virginia Medical Journal, Charleston

### 48:247-284 (Sept.) 1952

Diagnosis and Management of Diseases of Colon and Rectum. C. A. V. Burt.—p. 247.
Inguinal Hernia in Infancy and Early Childhood. J. T. Jarrett and B. Bradford Jr.—p. 253.
Teaching of Psychiatry: Its Place in Undergraduate Curriculum. S. Tait.—p. 256.
Recent Advances in Treatment of Leukemias and Lymphomas. G. E. Irwin.—p. 262.

### 48:285-312 (Oct.) 1952

Congenital Volvulus of Small Intestine. K. G. MacDonald.—p. 285.
People and Their Public Health. H. R. Leavell.—p. 289.
Cholecystography with Telepaque. V. L. Peterson.—p. 294.
Acute Aniline Poisoning. S. M. Jacobson.—p. 298.

## World Medical Association Bulletin, New York

### 4:193-256 (Oct.) 1952

World Medical Periodicals. H. Clegg.—p. 239.
Conflict Between Medical Profession and Social Insurance in Berlin. O. Leuch.—p. 240.
First World Conference on Medical Education. H. Clegg.—p. 241.
Medical Education an International Concern. L. Gerin-Lajoie.—p. 243.
First World Conference on Medical Education. H. G. Weiskotten.—p. 244.

## FOREIGN

### Australian and New Zealand J. Surgery, Sydney

**22:**1-80 (Aug.) 1952. **Partial Index**

Pancreatico-Duodenal Resection for Carcinoma. J. O. Smith and G. Brown.—p. 1.
*Malignant Melanomata: Some Points in Treatment and Prognosis. J. M. Clarke.—p. 8.
Benign Non-Traumatic Strictures of Bile Ducts. W. E. A. Hughes-Jones. —p. 14.
Sclerosing Peri-Angeitis of Lateral Thoracic Wall. E. S. R. Hughes. —p. 17.
Facial Neuralgias. R. A. Money.—p. 25.
Testicular Tumours: Association of Seminoma and Teratoma. E. S. J. King.—p. 32.
Pigmented Basal-Cell Tumours of the Skin. J. H. W. Birrell.—p. 47.
Malignant Synovioma with Special Reference to Diversity of Tissue Differentiation. G. G. Harkness.—p. 60.
Chronic Sclerosing Peri-Synovitis of Dorsum of Hand. G. McKenzie. —p. 70.

**Malignant Melanomas.**—It is impossible to advise excision of all pigmented moles or nevi, and Clarke feels that light brown moles may be left alone and that the hairy raised black patch rarely becomes malignant. The moles to be feared are the dark brown, black, or blue-black ones that are subject to trauma or irritations. Complete excision is the only advisable treatment. Diathermy, cautery, or carbon dioxide snow should not be applied, malignant changes having appeared after such treatment. Sections should not be taken out of a mole or suspected melanoma for microscopy unless the lesion is in a finger or a toe, where the alternative is amputation. When such a section is taken, a pathological report should be obtained with a minimum of delay. When a pigmented nevus or mole shows change of color, increase in size after a prolonged period with no apparent growth, or bleeding, it has almost certainly become malignant. The local lesion requires wide excision and the deep fascia should also be removed. The cutting diathermy may be used instead of the scalpel. It may not be possible to keep the wide margin of two inches from the lesion in certain sites such as the cheek, nose and eyelids, but the excision must be radical; if necessary, plastic surgery should be done in such cases. The accepted practice at present is to excise the regional lymph nodes radically within about six weeks of the excision of the primary lesion, whether they are clinically enlarged or not. The other possible course is to deal radically with the primary lesion and keep the patient under observation, excising the glands if they become enlarged. In a study of 90 cases of malignant melanoma at the Auckland consultation clinic between 1929 and 1946, the evidence is slightly in favor of local excision only for the primary lesion with delayed operation on regional lymph nodes as required. The prognosis in this series was considerably better in women than in men; it was also better in the younger age group. Lesions in the head area, in the digits, and in the leg appeared to have a better prognosis. It seemed that the shorter the period between apparent onset of malignancy and operation, the worse the prognosis. Smaller lesions seem to have a better prognosis than larger ones.

### British Journal of Venereal Diseases, London

**28:**105-158 (Sept.) 1952

Possible Applications of Adrenocorticotrophic Hormone (ACTH) and Cortisone in Syphilis. G. O. Horne.—p. 106.
*Gonococcal Infection of Para-Urethral Glands in the Female. E. Rees. —p. 115.
Newer Methods in Diagnosis and Treatment of Granuloma Inguinale. R. B. Greenblatt and W. E. Barfield.—p. 123.
Standardization of Wassermann Test Using Preserved Complement Titrated to 50 Per Cent Haemolysis. P. N. Coleman.—p. 129.
Syphilis in Mental Deficiency. W. V. Macfarlane and C. B. S. Schofield. —p. 138.
Aureomycin in Local Treatment of Trichomonas Vaginitis. C. S. Nicol, E. Gallagher and A. J. King.—p. 142.

**Gonococcal Infection of Paraurethral Glands in Women.**—Whereas in the early days of penicillin treatment of gonorrhea, cure rates of up to 100% were claimed after a single course of penicillin, recent reports suggest that the failure rate may be higher than was at first believed. The anatomical situation and histological formation of the paraurethral glands in women make them a potential focus of infection in gonorrhea. The frequent occurrence of signs of infection in these glands has been confirmed clinically by the finding of evidence of infection in 43 of the 92 cases reported. In 25 cases, signs relating to the paraurethral ducts occurred in the absence of clinical signs in the urethra, and in 22 of these 25 cases gonococci were found. Spread of infection throughout the glands is facilitated by the many forms of friction to which the glands are exposed. The resistance to treatment of infection of the glands has long been recognized; it would appear to result from the formation of small closed foci of infection due to blockage of the ducts by debris, and the conversion of these closed foci into intermittently draining foci by the friction to which they are subjected. It is, therefore, suggested that infection of the paraurethral glands is the cause of the persistence of gonococcal infection in many cases of relapse, and that in cases in which there are signs of chronic infection of the glands at the time of diagnosis, destruction of the glands, combined with systemic treatment is the quickest, and in some cases the only, method of affecting a cure. Some observers, including the present author, consider cauterization of the paraurethral glands more satisfactory than local application of penicillin.

### British Medical Journal, London

**2:**625-678 (Sept. 20) 1952

Statistical Aspects of Mortality in Early Adult Life. R. C. Geary.—p. 625.
Investigation into Comparative Efficacy of Certain Inhalants in Treatment of Asthma. E. Lewis-Faning and E. J. Parr.—p. 632.
Asthma in Childhood: Survey of Work of Asthma Clinic in Hampshire. C. B. S. Fuller.—p. 636.
Lymphangitis Carcinomatosa. G. N. Chandler and M. Telling.—p. 639.
Blood Glutathione Levels and Carbohydrate Tolerance During A.C.T.H. Therapy. C. L. Joiner.—p. 642.
*Streptomycin for Chronic Ambulant Tuberculous Patients. O. Clarke. —p. 644.
Acquired Hypersensitivity to Sodium P.A.S., Streptomycin, and Penicillin. B. Jeffery, P. Borrie and N. Macdonald.—p. 647.
Technique of Jelly (Tuberculin) Testing: Some Further Observations. J. D. Lendrum.—p. 649.

**Streptomycin for Chronic Tuberculosis.**—Streptomycin and *p*-aminosalicylic acid were given to 24 patients with pulmonary tuberculosis whose sputum was persistently positive on fluorescent microscopy or culture but who showed no other signs of clinical activity. Seven of these patients had chronic bilateral fibrotic disease that was too extensive for major surgery; 6 had a pneumothorax established for some months, but the sputum was consistently or intermittently positive; in 4 patients in whom thoracoplasty had been done, the sputum subsequently had been positive for at least a year; the remaining 7 patients had localized unilateral or bilateral fibrotic disease but were unsuitable for or had refused major surgery. All patients had been under observation for from six months to more than two years, before administration of streptomycin was begun. Streptomycin was given intramuscularly in doses of 1 gm. daily for 90 days, and *p*-aminosalicylic acid was given concurrently orally in doses of 14.1 gm. daily. The sputum of 23 patients became negative in the course of the treatment, and in 14 of them it remained negative up to two years. In five patients an isolated sputum specimen has been positive, but subsequent samples were negative. In four patients the converted negative sputum subsequently became again positive. The 24 patients continued their active work and social life during treatment, remaining economically independent and able to support their families without assistance. The results obtained in these patients showed that there is considerable scope for chemotherapy in selected patients with chronic disease whose only real disability is an infectious sputum that can be converted without interference with daily activities.

### Cardiologia, Basel

**21:**1-64 (No. 1) 1952. **Partial Index**

*Circulatory Dynamics in Patent Ductus Arteriosus and Problem of Pulmonary Arterial Hypertension. H. Denolin, J. Lequime and M. Segers.—p. 1.
Study of Time Derivative of Vectocardiogram. J. Shapiro.—p. 17.
Congestive Heart Failure with Bradycardia in Thyrotoxicosis. M. Rachmilewitz and A. M. Cohen.—p. 29.
Cardiac Complications of Xanthomatosis. S. Briskas, T. Doliopoulos and J. Laham.—p. 35.

**Circulatory Dynamics in Patients with Patent Ductus Arteriosus.**—Clinical and hemodynamic studies were performed in seven patients between the ages of 8 and 37 with patent ductus arteriosus. Six patients had normal pulmonary blood pressure and a

typical, continuous, blowing murmur. The seventh had a considerable rise of pulmonary blood pressure and a systolic murmur only. On roentgenologic examination the seventh patient showed pronounced hypertrophy of the heart, while in the other six the heart was normal or moderately enlarged. This rise of pulmonary blood pressure does not depend on the shunt produced by the patent ductus arteriosus. It is very likely primary and may result from a state of constriction in the small pulmonary vessels. Irreversible anatomic changes may be the final result of this hypertension. Patent ductus arteriosus is badly tolerated. During an exercise test, oxygen deficiency of the arterial blood may be manifested as well as a decrease of the ratio of oxygen consumed per liter of respirated air. Cyanosis and clubbing of the fingers may occur in certain cases. Electrocardiographic tracings were normal in four of the six patients with normal pulmonary pressure, while a slight right axis deviation was revealed in two. The patient with pulmonary hypertension showed a pronounced left axis deviation and a definite disturbance of conduction. There is no characteristic electrocardiographic pattern in patent ductus arteriosus; contrary to common opinion, right axis deviation is not unusual. There is no constant relation between the size of the shunt and the electrical axis deviation.

## Deutsche medizinische Wochenschrift, Stuttgart

**77:**1041-1106 (Sept. 5) 1952. **Partial Index**

Diagnosis and Treatment of Carcinoma of Rectum. R. Zenker.—p. 1041.
*Review and Present Status of Treatment of Subacute Bacterial Endocarditis. E. Boden and F. Loogen.—p. 1044.
Planned Use of Chemotherapeutics and Antibiotics with Aid of Resistance Determinations. H. W. Schlipköter.—p. 1049.
Diet in Treatment of Diffuse Acute and Chronic Lesions of the Parenchyma of the Liver. H. Kalk and E. Wildhirt.—p. 1052.
*Clinical Aspects of Myocardial Infarction with Particular Consideration of Use of Anticoagulants. H. Zapfe and P. Sonnenberg.—p. 1054.
Hormones of Adrenal Cortex in Treatment of Heart Disease. F. Pendl.—p. 1057.
Action of Khellin on Urinary Organs. E. Gadermann.—p. 1067.
Care of the Newborn of Diabetic Mothers. W. Heck.—p. 1069.
Human Globulin in Treatment of Herpes Zoster. H. Gros.—p. 1074.

**Treatment of Endocarditis Lenta.**—Since 1946 the authors have treated 108 patients with endocarditis lenta but because they feel that at least three years have to elapse before final evaluation is possible, they have evaluated chiefly the 71 treated between 1946 and 1948. Thirteen of these, or 18%, can be regarded as definitely cured. This percentage of success is much below that reported in the Anglo-American literature. This may be partly explained by the restricted supply of penicillin available to these investigators, but even in recent years, when penicillin therapy has been more intense and prolonged, the therapeutic results have not been greatly improved. A difference between the concepts of endocarditis lenta and of subacute bacterial endocarditis may be another factor explaining the differences in results obtained in Germany and Anglo-American countries. A third factor may be the discrepancy between the frequency of the demonstration of the causal organism in the Anglo-American countries and in Germany, as well as the different attitude toward the treatment with antibiotics in cases in which the causal organism has or has not been demonstrated. Finally the concept of "cure" of endocarditis is different in these countries from that accepted by these authors. Treatment with penicillin is the best form of therapy. If it alone is not effective, combination therapy with penicillin plus streptomycin should be tried. Aureomycin, terramycin and chloramphenicol (chloromycetin®) are much less effective in endocarditis than penicillin and streptomycin. The authors warn against the combination of these newer antibiotics with penicillin or streptomycin because of "antibiotic antagonism." The authors stress the importance of removal of foci of infection, mention the combination treatment of penicillin with proteins of nonpathogenic bacteria, and finally discuss the use of amithiozone and its mode of action.

**Use of Anticoagulants in Myocardial Infarction.**—Zapfe and Sonnenberg review the electrocardiographic and clinical observations in 89 patients who were hospitalized because of an acute myocardial infarction. Some of these were given anticoagulants in addition to the customary treatment. An attempt was made to ascertain whether the use of anticoagulants influences thromboembolic complications and the mortality. The authors feel that anticoagulants do not become effective until from 48 to 72 hours after onset of their administration. Of 29 patients who died, 13 died within this period and none of these died as the result of a thromboembolic complication. Thus there remain for comparison 33 who were given anticoagulants, mostly bishydroxycoumarin, and 43 who were not. Thromboembolic complications occurred in 3.3% of the treated group, and in 16% of the group not given bishydroxycoumarin. The authors feel that these observations, like reports on larger numbers of cases in the United States, indicate that administration of anticoagulants reduces thromboembolic complications. If the prothrombin level is followed carefully, the danger of serious hemorrhagic complications is slight. Only comparatively young patients with anterior septal primary infarcts should be exempted from treatment with anticoagulants, because in such cases the infarcts are comparatively mild and take a favorable course.

## Edinburgh Medical Journal

**59:**409-456 (Sept.) 1952

Surgical Emergencies of Infancy. F. H. Robarts.—p. 409.
Observations on Aetiology of Bronchiectasis. N. Wynn-Williams.—p. 427.
Carotid Sinus Syndrome and Carotid Body Tumour. W. Michie and R. G. Simpson.—p. 443.

## Lancet, London

**2:**545-592 (Sept. 20) 1952

Miliary Tuberculosis in Children. R. Debré.—p. 545.
Infectiousness of Communicable Diseases in Household (Measles, Chickenpox, and Mumps). R. E. Hope Simpson.—p. 549.
Inadvisability of Giving A.C.T.H. to Patients with Gastric Ulcer. J. Forbes.—p. 555.
C-Reactive Protein in Rheumatic Fever. A. G. S. Hill.—p. 558.
Shock in Botulism Treated with Dextran and Blood. J. Pedersen and A. Christensen.—p. 560.
Simple Paper Chromatographic Technique for Amino-Acid Analysis of Blood. K. V. Giri, K. Krishnamurthy and T. A. Venkitasubramanian.—p. 562.
Hysterosalpingography: To Screen or Not to Screen. W. G. MacGregor and R. Oliver.—p. 563.
Secondary Steatorrhoea Following Gastro-Ileal Anastomosis. D. W. Barritt.—p. 564.
Post-Mortem Caesarean Delivery After Rupture of Dissecting Aortic Aneurysm. J. T. Spenser.—p. 565.

## Maandschrift voor Kindergeneeskunde, Leyden

**20:**249-288 (Sept.) 1952

Effect of Intravenous Injection of Suspensions of Blood Platelets in Disorders Characterized by Thrombocytopenia and Thrombopathy. S. van Creveld, M. M. P. Paulssen and H. L. J. M. Bartels.—p. 249.
*Retrolental Fibroplasia in the Netherlands. C. H. O. M. von Winning.—p. 268.
*Retrolental Fibroplasia and Oxygen. J. T. Swart-van der Hoeven and T. M. B. Mak.—p. 276.
Cure of Waterhouse-Friderichsen Disease with Corticotropin (ACTH): Report of a Case. C. Smeenk.—p. 286.

**Retrolental Fibroplasia in the Netherlands.**—A total of 30 cases of retrolental fibroplasia have been reported in the Netherlands in the last four years. The symptomatology of the condition is described and the incidence in various countries compared. The histories of premature uniovular twins who had retrolental fibroplasia are presented. These suggest that an oversupply of oxygen may be the most important factor in the pathogenesis of this disorder. The smallest of the twins had the mildest form of retrolental fibroplasia. In this twin, who had considerable cyanosis, presumably the oxygen treatment was not so excessive as in the larger twin, who was only slightly cyanotic. Consequently, when oxygen therapy was discontinued, the rapid reduction in oxygen concentration produced severer anoxia and retrolental fibroplasia in the larger of the twins. The author stresses, that the oxygen supply in incubators for premature infants must be carefully controlled. Factors that play a part in anoxemia, such as anemia, must be watched for in prematurely born infants. Ophthalmologic follow-up of such infants is very important.

**Retrolental Fibroplasia and Oxygen.**—In connection with observations on two prematurely born infants with retrolental fibroplasia, the authors review the etiological theories that have been suggested with regard to this disorder, such as the possible role of vitamin A and vitamin E. Australian observers first

noted a connection of this disorder with the use of incubators providing high oxygen tension for prematurely born infants, and Szewcyk in the United States also noted the role of oxygen therapy in this disorder. In comparing their own observations on the effect of giving oxygen and then omitting oxygen therapy in retrolental fibroplasia, however, the authors find that the changes induced by administration of oxygen and the interruption of this therapy are not as spectacular as suggested by Szewcyk. Nevertheless, they too are convinced of the role of oxygen therapy in this disorder, especially since one of their own two patients was a twin in whom signs of retrolental fibroplasia advanced and regressed with oxygen therapy, whereas the second twin who received no oxygen therapy retained normal ocular fundi. The authors make the following recommendations: 1. Prematurely born infants should be given oxygen only if it is definitely indicated by cyanosis or superficial and irregular breathing. If it is given, it should be given at a low tension and should be discontinued as soon as possible. 2. The eyes of infants who have received oxygen treatment should be examined several times per week during and after such treatment. 3. Acclimatization to lower oxygen tensions should be gradual and slow.

## Medicina, Buenos Aires

**12:123-190 (June) 1952. Partial Index**

*Chronic Chagas' Heart Disease. A. C. Taquini, B. B. Lozada and B. Furman.—p. 123.
*Epilepsy in Twins. C. Castells and B. Fuster.—p. 149.
Syphilitic Aortitis and Pulmonary Arteritis. (Syndrome of Inverted Isthmic Coarctation and Pulmonary Arterial Hypertension). A. Agrest, A. J. Roncoroni, A. Lerner and M. Finkelstein.—p. 158.

**Chronic Chagas' Disease with Heart Involvement.**—Recent studies have shown a high incidence of chronic Chagas' disease in Argentina, where the disease is endemic over large areas. Cardiac disturbances caused by the localization of this disease in the heart become increasingly severe with the passage of time, causing symptoms of dyspnea and edema in many cases, and often ending in sudden death. Diagnosis must be based on a history of residence or temporary visits in regions where the disease is endemic, especially if triatoma bugs were present in the patient's living quarters; on electrocardiographic changes; on a positive complement fixation reaction; and on cardiac insufficiency (when present) characterized by chronicity and the fact that it is generally well tolerated. Clinical, radiological, electrocardiographic, and laboratory study of 12 patients with chronic Chagas' disease of the heart showed that electrocardiographic changes provided the most striking evidence of the inflammatory myocardial process. Disturbances of rhythm occurred in 11 cases, ventricular extra systoles being the most frequent. Other pictures presented were those of sinoauricular heart block, complete auriculoventricular heart block, auricular fibrillation, and bundle-branch block, with right bundle-branch block predominating. Changes were also found in the QRS and T waves. The variety of the electrocardiographic changes shown simultaneously in a single tracing, indicating the existence of a diffuse myocardial process, was the most striking feature found on examination, and the fact that the picture presented was similar in most cases gives it increasing importance as a diagnostic sign. The discrepancy between the gravity of the electrocardiographic changes and the rest of the clinical picture indicates that a finding of bundle-branch or auriculoventricular heart block without obvious etiology should arouse suspicion of Chagas' disease with myocardial localization. The complement fixation reaction was positive in all cases in which the test was made. Asymptomatic cases of this condition have been reported, and two of the patients in this series were free from cardiac symptoms; the other 10 had symptoms of varying intensity. There were three deaths: two occurred suddenly and one was caused by intercurrent disease. Pathological findings in these three cases consisted of total cardiac enlargement, diffuse chronic myocarditis, and myocardial degeneration with histiocytic, monocytic and lymphocytic infiltrates in the interstices.

**Epilepsy in Twins.**—Some authorities believe that epileptic attacks may be caused by both genetic and acquired factors, acting separately or together, others deny the influence of heredity altogether, and still others accept it in all cases. The fact that the number of cases in which both twins, whether monozygotic or bizygotic, are epileptic is greater in idiopathic than in symptomatic epilepsy indicates not only that the genetic factor is important but also that it is capable of producing epilepsy in the absence of any acquired factor. Symptomatic epilepsy is exceptional in both bizygotic twins, whose heredity may be dissimilar, but is occasionally found in both monozygotic twins, indicating that in such cases the two factors act together, the hereditary factor causing an epileptogenic predisposition and the acquired factor serving as the irritant. Six pairs of twins were studied with special reference to the clinical and electroencephalographic characteristics of genetic and acquired epilepsy; of these, four pairs were bizygotic, one was certainly monozygotic, and one was probably so. Both twins in the unquestionably monozygotic pair were epileptic; in the other pairs only one twin was epileptic. The grand mal attacks and bilateral, symmetrical, and synchronous epileptiform activity shown in the electroencephalograms of the two monozygotic twins were of the type caused by activation of the subcortical structures, commonly seen in idiopathic epilepsy. Normal neurological findings and a history completely negative for acquired factors indicated that the epilepsy in this case was due to a genetic factor acting alone. The cause of the epilepsy in the affected twin of the pair that was probably monozygotic could not be determined, but various circumstances indicated it to be symptomatic of an undetected cerebral lesion. The findings in the bizygotic pairs, in which one twin was affected and one was normal, showed that epilepsy may also be produced by an acquired factor in the absence of any inherited epileptogenic predisposition.

## Minerva Chirurgica, Turin

**7:535-562 (July 31) 1952. Partial Index**

*Valvotomy Knife for Mitral Commissurotomy. A. M. Dogliotti and G. Guglielmini.—p. 535.
*Mechanism of Traumatic Rupture of Spleen. M. Pompili.—p. 536.
Cystic Dilatation of Choledochus: One Case. G. Gili.—p. 539.
Clinically Primary Axillary Metastases in Latent Carcinoma of Breast: One Clinical Case. C. Massimo.—p. 541.

**Knife for Mitral Commissurotomy.**—The authors have designed a small knife blade attached to a finger ring for use in commissurotomy of the mitral valve in mitral stenosis. The ring, made to fit over the base of the nail of the right index finger, is cut out over the dorsal aspect so that the diameter of the finger is not increased while the ring is being worn. On the ventral aspect there is a sharp semilunar blade 3 to 4 mm. long. During the operation the right index is at first introduced into the left atrium through the auricle without the ring, and an attempt is made to widen the mitral orifice by digital dissection alone. When two valvular commissures cannot be sufficiently separated with the finger alone, this is withdrawn and while the auricle is closed with a compressor, the ring and a second thin rubber glove are put on the right hand. The sharp blade cuts the glove and it is the only part that protrudes from the glove. The finger is introduced again into the atrium with the blade facing the commissure. This is cut by the blade when the finger forces its entrance into the mitral orifice. This process may be repeated several times. When the posteromedian commissure also needs cutting, the glove is removed and the ring is rotated through an angle of 180 degrees.

**Rupture of the Spleen.**—Spontaneous rupture of the normal or diseased spleen may occur as a result of crushing or lacerating trauma, severe compression, excess flexion, or forced extension. The type of disease is of great importance. The spleen ruptures more easily in patients with malaria than in those with tuberculosis and leukemia. Today, because of the type of work and the emphasis on sports, rupture of the spleen seems to occur often. The structure of the organ also plays an important role: fragility of the parenchyma and excess blood circulating in the spleen with changes in pressure, are factors predisposing to its rupture. The author reports three cases of traumatic rupture of the spleen in boys from 11 to 18 years of age. In two of them the spleen was normal, and the other patient had splenomegaly due to malaria. In two patients the diagnosis was easy because there were signs of sudden internal hemorrhage and objective signs of rupture of the spleen were present. In the other patient at the time of hospitalization, six to eight hours after the trauma, there were no signs of acute anemia or ab-

dominal bleeding. After more than 48 hours signs of profuse internal hemorrhage appeared. Delayed hemorrhages like this occur either because at first the rupture is only subcapsular and the increase of the intrasplenic hematoma leads to distension of the capsule to the point of bursting, or because a temporary spontaneous hemostasis occurs due to spasm of the vessels, obstruction of the omentum, and formation of a perisplenic hematoma. The spleen was removed under general anesthesia in two patients and under local anesthesia in one. All of them recovered.

## Presse Médicale, Paris

**60:**1231-1250 (Sept. 24) 1952

Nelson and Mayer's Test; New Clinical and Experimental Research. C. Levaditi, A. Vaisman and A. Hamelin.—p. 1231.
Action of Hypocalcemia on Ventricular Electrocardiogram; Comparative Physiopathological Study. F.-P. Merklen, P. Berthaux and J. Forman. —p. 1233.
*Clinical and Experimental Study of Para-Aminosalicylic Acid Preparation for Prolonged Action (Its Association with Intravenous Infusion of PAS). A. Duroux, R. Verges-Breton and J. Desbordes.—p. 1236.

**Para-Aminosalicylic Acid Preparation for Prolonged Action.**—The effectiveness of *p*-aminosalicylic acid in the treatment of pulmonary tuberculosis depends on the concentration of the drug in the blood of the patient. Comparison of concentrations obtained by various routes of administration showed that the highest blood levels were obtained with intravenous infusions. This high concentration, however, was of short duration, and parenteral administration is not always possible, particularly if the patient is not hospitalized. Oral administration of doses large enough to maintain adequate concentration of the drug in the blood was always limited by digestive disturbances due to intolerance of the drug. Experiments with variable doses of *p*-aminosalicylic acid showed that the optimum therapeutic concentration of the drug is about 60 mg. per 1,000 cc. of serum. Therapeutic trials with a new *p*-aminosalicylic acid preparation containing *p*-aminosalicylic acid sodium, pectin, vitamin C, and certain flavine derivatives from orange peel gave satisfactory clinical and roentgenologic results with moderate doses administered by mouth. The absence of any digestive disturbances made continuation of the treatment for four months possible. The optimum concentration of *p*-aminosalicylic acid in the blood could be maintained for eight instead of only three hours by using combined administration routes, namely intravenous infusion followed by oral administration of the new preparation three hours later when the drug was being eliminated most rapidly but before its concentration in the blood had dropped below 60 mg. per 1,000 cc. Of five patients with recent cavities and Koch's bacilli in the sputum, four obtained closure of the cavities and disappearance of the bacilli from the sputum within six weeks. In the fifth patient, a cavity of five months' duration was considerably diminished in size within three weeks, making establishment of an extrapleural pneumothorax possible.

## Progresso Medico, Naples

**8:**449-480 (Aug. 15) 1952. **Partial Index**

Modifications in the Metabolism of Vitamins and Phosphoric Esters of Carbohydrates in Relation to Changes in Phosphorylation Processes in Diabetes. L. Travia.—p. 451.
*Problems of Genetics in Diabetes Mellitus. A. Iannaccone, A. W. D'Agostino and M. Siniscalco.—p. 457.

**Genetics in Diabetes Mellitus.**—The hereditary factors and the age of onset of diabetes mellitus were studied in 47 Neapolitan families in which all the siblings of the probands were over 60 years of age. It was revealed that when the diabetic was the offspring of two healthy parents the disease was found in the collaterals of one of them. In some cases in which one parent was healthy and the other diabetic the disease was found in the collaterals of the healthy parent. Direct transmission from the parents to the children was found only in the first generation. Juvenile diabetes was rare and limited to children of two nondiabetic parents. These findings seem to confirm the hypothesis of recessive inheritance. In studying the age of onset of the disease in pairs of siblings it was found that the different age is attributable to modifying genes that influence the main gene of diabetes. In a genetic analysis of these modifying genes there was evidence that they were not linked to sexual chromosomes. The authors cited the first results of a study that is still in progress to investigate whether the diabetes gene is linked to another autosomal gene in the same chromosome. If this is true and if the presence of this second gene can be ascertained sooner and more easily than the gene of diabetes, it will be possible to detect the disease in those carriers in whom the disease has not as yet manifested itself.

## Revista Medica de Chile, Santiago

**80:**323-398 (June) 1952. **Partial Index**

Experience with Cardiac Catheterization. R. Armas Cruz, F. Rojas Villegas and P. Falgerete.—p. 323.
Experience in Connection with Obstetric Advances in the Last 15 Years. V. M. Aviles B.—p. 333.
*Studies in Prostate Cancer in Relation to Its Hormonal Treatment. Determination of 17-Ketosteroids and Eosinophil Count. H. Acevedo, J. Zanartu, A. Atria R. and C. Lobo Oneil.—p. 350.
Headache and Hypertension. R. Guzman and H. Serani.—p. 356.

**Cancer of the Prostate and Hormone Treatment.**—Twenty-two patients with cancer of the prostate, some with metastases and some without, were studied in relation to excretion of total neutral urinary 17-ketosteroids and the circulating eosinophil count. Determinations of the 17-ketosteroids in all 22 patients, none of whom was at the time receiving any treatment that might affect the result, indicated that the total excretion of these catabolites is generally normal in cases of prostatic cancer. The decline in the number of circulating eosinophils in response to the epinephrine test in most of eight patients similarly free from treatment affecting the result also suggested normal functioning of the adrenal cortex in this disease. Thirteen of the patients underwent orchidectomy, and in nine of these the 17-ketosteroid excretion rate was determined before and at least one month after operation. The results indicated a postoperative reduction of about one-third as compared to the preoperative rate, but even so the figures were in most cases still within limits considered normal. Response to the epinephrine test in six patients in this group was normal in two and subnormal in the other four. Finally, the 17-ketosteroid excretion rate was studied in 12 patients treated with subcutaneous implants of diethylstilbestrol, 8 of whom had undergone orchidectomy. Definite reduction resulting in clearly subnormal excretion rates was found in the castrated patients; in all but one of the others the reduction was less pronounced, the values being close to the lower limit regarded as normal in each individual case. The epinephrine test in seven cases showed results that were positive in four, doubtful in one, and negative in two. These studies indicate that neither the determination of the 17-ketosteroid excretion rate nor the epinephrine test has any diagnostic value, but that determination of the 17-ketosteroids is useful in measuring the restraining or inhibiting effect of the adrenal cortex.

## Schweizerische medizinische Wochenschrift, Basel

**82:**913-936 (Sept. 13) 1952. **Partial Index**

Hypothyreosis. M. Richard.—p. 913.
*Experiences with Penicillin Therapy in Neurosyphilis. G. Miescher and H. Brenn.—p. 917.
Arterial Oxygen Deficiency. E. Jéquier-Doge and K. Wiesinger.—p. 923.

**Penicillin Therapy in Neurosyphilis.**—Of 70 patients with neurosyphilis treated with penicillin at the dermatological clinic in Zurich between 1947 and 1951, 17 had progressive paralysis, 20 taboparesis, 11 tabes dorsalis, 13 meningovascular syphilis, and 9 asymptomatic neurosyphilis. Of the 70 patients 35 had not received any previous treatment while the other 35 patients had been given arsphenamine and bismuth combined with fever therapy during the primary and secondary stages of syphilis and 25 of them had been treated twice before the neurosyphilis was detected. In this study, 48 patients were given penicillin combined with oxophenarsine hydrochloride (mapharsen®), bismuth and fever therapy, and 22 patients were treated with penicillin alone. Up to 1949 penicillin was given in aqueous solution every three hours for seven and a half to 10 days in total amounts of 2,000,000 to 4,800,000 units. After 1949, repository penicillin was employed. At first 6,000,000 units were given in 10 days. Later 600,000 units were given three times a week for eight weeks, with a total dose of 14,400,000 units. Thirty patients received one course of treatment and 40 were given several

courses. Follow-up varied from one to four years. Results showed that penicillin is effective in all types of neurosyphilis, and that it is almost as effective as malariotherapy. Of the 70 patients, 53 had their work capacity fully restored, work capacity was limited in 7, and 10 were not able to work. The greatest improvement of cerebrospinal fluid and of clinical symptoms occurred in those who had the most active process at the beginning of treatment. Combined treatment with arsphenamine and bismuth did not offer any advantages. The possible occurrence of a Herxheimer reaction must be considered in patients with greatly increased cell count and abnormal albumin values, and particularly in those with progressive paralysis. In the presence of this complication, continuation of the treatment seems to offer greater advantages than discontinuation. Preparatory treatment with a few injections of bismuth does not prevent the occurrence of a Herxheimer reaction, while prolonged treatment with bismuth for six weeks, or preparatory malariotherapy seems to be more effective in this regard. The authors conclude that besides malariotherapy penicillin takes the first place in the treatment of neurosyphilis and that treatment with penicillin exclusively seems to be justified.

## Ugeskrift for Laeger, Copenhagen

**114:**1087-1124 (Aug. 14) 1952

*Microcystic Basal Cell Carcinoma, Particularly in Upper Respiratory and Alimentary Passages: Clinical Investigation. H. B. Mathiesen.—p. 1087.
*Acute Benign Pericarditis. J. Gormsen.—p. 1096.
Malignant Tumor Formation in Chronic Osteomyelitis. G. Munk-Andersen.—p. 1101.
Continued Experiences in Treatment of Clubfoot by Denis Browne's Method. J. Agerholm-Christensen and W. Permin.—p. 1103.
Roentgen Examination of Colon in Acute Abdominal Disorders: Value of Routine Roentgen Examination of Colon in Patients Admitted for Observation for Acute Abdominal Disorders. T. Hølund.—p. 1104.
Fordyce's Disease (Sebaceous Glands in Buccal Mucous Membrane). C. L. S. Bohn.—p. 1105.
Investigations on Effect of "Glare-Free" Glasses for Motorists. C. L. S. Bohn.—p. 1107.
Tuberculosis Examinations of Personnel Attached to Copenhagen Schools 1944-1950. K. Bojlèn.—p. 1108.
Treatment of Herpes Zoster with Posterior Pituitary ("Pituitrin") Preparations. K. Secher.—p. 1109.

**Microcystic Basal Cell Carcinoma.**—Mathiesen's material comprises 94 cases from the literature, including 10 personal cases. Microcystic basal cell carcinoma (cylindroma) may be regarded as a special form of tumor that tends to develop in the nose and nasal sinuses, palate, larynx and trachea; a rare localization is the ear and mastoid process. Growth is slow, often extending over years. The symptoms depend on the localization. In the nose and its sinuses there is a striking progression with spread to the adjacent structures. Cases in the larynx and trachea may be wrongly diagnosed for years. In two-thirds of the cases there is local recurrence after treatment. The most frequent metastases are to the lungs and regional glands, but there are no metastases in three-fourths of the cases. Microcystic basal cell carcinoma requires radical surgical treatment, which necessitates close cooperation between the histologist, surgeon, and roentgenologist. The author advises postoperative local radium packing in the cavity if possible, or postoperative roentgen treatment. The mortality after treatment is about 33%. The personal cases are described.

**Acute Benign Pericarditis.**—Gormsen reports seven cases of acute, benign, nonspecific pericarditis, in six men and one woman, that resemble the cases described in the American literature. Electrocardiographic examination showed the classic changes of acute pericarditis. In two cases roentgenograms revealed an enlarged heart shadow, which regressed rapidly, in two cases, pneumonitis, and in one case, pleural effusion. The disorder affects mainly males aged from 15 to 45. It begins with elevation of temperature, pronounced initial pain, which is usually precordial but occasionally is localized in the epigastrium, lower abdomen, back, right side of chest, or shoulder (oftener the left shoulder), radiating into arms and fingers. The definite pericardial friction rub is important in the diagnosis. The immediate prognosis is good. The etiology is unknown. The effect of antibiotics cannot readily be judged, as there is a marked tendency to spontaneous regression. Penicillin and sulfonamide preparations are not effective. A similar disorder, "epidemic pericarditis," was reported by Bing in 1933.

## Zentralblatt für Chirurgie, Leipzig

**77:**1249-1296 (No. 30) 1952. **Partial Index**

*Conservative Treatment of Acute Necrosis of Pancreas by Procaine Hydrochloride Block. K. Klumpp.—p. 1249.
Genuine Liver Cyst. J. Jáki.—p. 1260.
Diverticulosis of Jejunum. W. Hahn.—p. 1263.
Ossification of Periosteal Flap in Surgical Correction of Flatfoot. K. Schlüter.—p. 1270.
Rare Case of Chondroma of Shoulder-Joint. K. Schiltenwolf.—p. 1274.

**Sympathetic Ganglion Block for Necrosis of Pancreas.**—Infiltration of the paravertebral and prevertebral sympathetic ganglions at the level of the 12th thoracic vertebra with 40 to 50 cc. of a 0.75% solution of procaine hydrochloride and potassium sulfate was carried out in 15 patients with acute necrosis of the pancreas. A sudden drop of the diastase in the urine resulted within several minutes to a few hours after the sympathetic block. This striking effect of the block was accompanied by improvement of the general condition. Pain disappeared rapidly, normal function of intestines was restored, and leukocytes decreased. Before the ganglion block all the patients had hyperglycemia without glycosuria; within 14 days after the block the blood sugar level was restored to near normal. Conservative treatment by sympathetic ganglion block thus proved superior to any surgical treatment of acute necrosis of the pancreas. One of the possible mechanisms in the production of acute necrosis of the pancreas is a disturbance of blood flow within the pancreas. Blood flow is regulated by the autonomic nervous system, and the ganglions of the sympathetic nerve play an important part in this process. Inflammation of the bile ducts, disease of the duodenum or of the appendix, or other foci of infection may cause irritation of the autonomic nervous system in the area of the celiac ganglion. By restoring normal sympathetic tonus procaine hydrochloride infiltration of the sympathetic ganglions not only influences favorably the disturbed circulation but apparently also the cause of the disease, as is suggested by the rapid drop in urinary diastase and the associated clinical improvement.

## Zentralblatt für Gynäkologie, Leipzig

**74:**1249-1280 (No. 32) 1952. **Partial Index**

*Question of Malignancy of Granulosa Cell Tumors. H. Muth and P. Stoll.—p. 1249.
Role of Excessive Folliculinization in Pathogenesis of Carcinoma of Corpus Uteri. W. Walz.—p. 1256.
Development of Polymorphocellular Sarcoma of the Vermiform Appendix After Removal of Papillary Carcinoma of Ovaries. F. Isbruch.—p. 1269.

**Malignancy of Granulosa Cell Tumors.**—Most investigators consider granulosa cell tumors as relatively benign ovarian neoplasms, since they rarely cause destructive infiltrations or metastases beyond the limits of the ovary. For this reason, conservative surgical methods are generally regarded as adequate. Other investigators, however, assert that granulosa cell tumors are definitely malignant. At the clinic with which the authors are connected, four malignant granulosa cell tumors were observed in one year. These four patients had a brief history of symptoms, which did not suggest the advanced stage of the tumor. Growth was extremely rapid. Surgical treatment was resorted to, because a malignant tumor was suspected. That the neoplasms were granulosa cell tumors was ascertained by morphological examination of the surgical specimens. The severe degree of malignancy was proved by the condition found at operation, by the further unfavorable course, by bilateral spread in three cases, by extension beyond the ovary in all four cases, and by presence of metastases not only in the abdomen but, in one case, even in the skeletal system. Theses cases induced the authors to review the records of their clinic. Among a total of 25 cases of granulosa cell tumors, four malignant cases were found, and in one case a relapse occurred after five years. The malignant tumors always occurred in sexually mature women. Histological or cytological evaluation of malignancy and the presence or absence of histological function cannot be relied on for prognostic evaluation. Only the clinical course permits differentiation of the highly malignant form with rapid course and metastasis, which suggest ovarian carcinomas, from the less malignant form with slow growth and perhaps late metastasis. These tumors, because of their hormonal function, cause abnormal bleeding and may be correctly diagnosed before operation. The occurrence of a third, benign form with a tendency to retrogression (fibromatous transformation) must be assumed.

# BOOK REVIEWS

**The History and Development of Neurological Surgery.** By Ernest Sachs, A.B, M.D., Research Associate in Physiology, Yale University, New Haven. Publication no. 29, Department of History of Medicine (formerly monograph series of Historical Library) Yale University School of Medicine. Cloth. $5. Pp. 158, with 50 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1952.

This is the third monograph that has recently appeared in this country on the history of neurological surgery. Like the others, it has been prepared by a well-informed, well-known, respected member of the specialty. The book is arranged in chronological order. It emphasizes the importance of physiological studies and of other basic sciences to the development of this clinical field. Dr. Sachs was a pupil of the great English neurophysiologist and neurosurgeon Sir Victor Horsley. He was one of the early neurosurgeons in the United States and did much to develop this field, especially in the Middle West. All those interested in the development of neurological surgery and the history of medicine will enjoy this authoritative little book. The photographs of those who have been outstanding in the progress of this field will be particularly appreciated. There is an extensive bibliography of 540 entries and a thorough index.

**The Application of Scientific Methods to Industrial and Service Medicine.** (Proceedings of conference held from March 29th to March 31st, 1950). Medical Research Council. Paper. 3s. Pp. 112, with illustrations. His Majesty's Stationery Office, Box 569, London, S.E.1, 1951.

This book is the report of a two-day conference organized as an experiment to bring together groups of physicians working in industry and in the services. There is a discussion of the application of statistics to analysis of data obtained in field surveys, and another concerned with the requirements for study of sickness incidence on the job. Field surveys in industry and the services are compared in relationship to laboratory research. Another topic discussed is the study of human performance in relation to safety and health as these may be influenced by the working environment and temperature. Sir Frederick Bartlett discusses the laboratory approach to the study of problems involving mental and bodily skill. Other papers deal with subjects more directly concerned with industry, such as dust diseases of the lung and the various approaches to this subject. Fluorosis and berylliosis are discussed, as well as the occupational and domiciliary factors in tuberculosis.

**Chemical Physiology of Endoparasitic Animals.** By Theodor von Brand. Cloth. $7.50. Pp. 339. Academic Press, Inc., 125 E. 23rd St., New York 10, 1952.

The author hoped that by critically reviewing the scattered literature he could focus the interest of the biochemists on the neglected field of endoparasitic animals. He addresses himself to graduate students with preliminary training in both parasitology and biochemistry and to investigators interested in some particular phase of parasite physiology.

The work is divided into three main sections dealing with the chemical composition and the metabolism of endoparasites and with chemical host-parasite relationships. In this last section the individual chapters cover nutritional relationships, the physiological basis and metabolic consequences of parasitic anemias, metabolic disturbances in hosts, endocrine relationships, and chemotherapy as related to parasite physiology (selection of drugs and the problem of drug resistance). Comparatively little work seems to have been done on man, and, moreover, the information given that affects clinical medicine is already well known to the medical profession, so that on both these counts the work will have a limited appeal to physicians. The writing is good, the bibliographies and indexes are extensive and apparently accurate, and the makeup is splendid.

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The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

**Nursing Care of Communicable Diseases: Prophylactic Technics for the Prevention and the Control of Disease.** By Mary Elizabeth Pillsbury and Elizabeth Johanna Sachs. Science adviser and editor: Jean Broadhurst. Contributors: Jessie Wright and Jane Taylor Torrance. Seventh edition. Cloth. $4.50. Pp. 843, with 149 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1952.

This edition has been entirely rewritten. Part 1 stresses the importance of a groundwork in microbiology, immunity, and community phases of disease prevention and disease control. A chapter has been added on chemotherapy. Part 2 is devoted to the communicable diseases. The discussion of each disease is introduced with a statement on definition, history, and present occurrence. Then follows the medical aspect, with a discussion of etiology, source, transfer, incubation period, communicability, laboratory diagnosis, course and prognosis of the disease, treatment, and measures for control. This is followed by the nursing aspect, which emphasizes the nurse-patient relationship in such aspects as care and comfort of the patient, recognition of complications, and special isolation and disinfection recommendations. Part 3 includes a brief review of the history of hospital and public health care of communicable diseases. In part 4 are discussed disinfection procedures, general references, audio and visual aids, a program of clinical instruction in communicable disease nursing, and 148 situation questions. These questions are included in a separate section and cover not only the actual care of recognized diseases but also public health aspects. These are a sampling of the newer aspects of examinations for the R.N. degree.

Each chapter is followed by a list of references. Stress is laid throughout the book on the role of the nurse as a teacher of health. Emphasis is placed also on patient care both in the home and in the hospital. The book should provide an excellent background textbook for the student nurse. The author states, however, that in such a rapidly changing field as communicable diseases no text can long remain truly up-to-date and should be supplemented continually by new nursing and medical journals.

**Roentgenology in Obstetrics and Gynecology.** By William Snow, M.D., Chief Radiologist, Veterans Hospital, Shreveport, Louisiana. [Second edition of Clinical Roentgenology of Pregnancy.] Cloth. $10.50. Pp. 363, with 273 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1952.

This brief and yet comprehensive textbook is well written and contains excellent illustrations and plates. It is based largely on the author's studies since 1949 of 12,000 pregnancies, including pelvic measurements, pelvic architecture, the maternal soft parts, and fetal measurements. A simple substitution for the Caldwell-Malloy classification of the female pelvis is presented. There is an excellent discussion of the common pelvic types and their relationship to the mechanism of labor. The factors involved in the normal positions of the presenting part and their changes during the course of labor are discussed from the standpoint of the uterus, placenta, pelvic inlet, sacrum, and pelvic floor. Included is a discussion of the normal and the asymmetrical bony pelvis. Fetal death and the caution that must be exercised in its roentgen diagnosis are discussed. Along with this is a brief discussion of common fetal anomalies, congenital infections such as syphilis and toxoplasmosis, and common fetal injuries that are sustained during labor. The use of Ball's method for estimating the skull size is discussed here and earlier, under the mechanism of labor, and it is mentioned with some caution that the biparietal and suboccipital bregmatic diameters of the skull may be used to estimate the fetal age in weeks.

In the discussion of the maternal soft parts, the variation in placental position is well covered, but the theoretical causes and the treatment of polyhydramnios could well have been omitted, as well as the discussion regarding the length of the vaginal canal and the placement of the diaphragm pessary. There is an excellent discussion of extrauterine pregnancy and the value of roentgen diagnosis of this condition, as well as a very good brief discussion of uterine salpingography. In the absence of

better theoretical proof, the discussion of the mechanical and hormonal dilatation of the upper urinary tract, as well as the section describing contraction of the calices and pelvis of either kidney due to reflex narrowing related to irritation of the urinary tract, would probably better have been omitted. The remaining chapters are brief but to the point. The book contains adequate bibliographies; the author's style is easily read; and the material is presented with unusual clarity.

**Rorschach's Test. III: Advances in Interpretation.** By Samuel J. Beck, Ph.D. Cloth. $5.50. Pp. 301. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1952.

This book reports the advances in interpretation that the author has made since the publication of the preceding volume in 1945. These advances have been both quantitative and qualitative, the former being derived from two research projects carried on by the author and the latter from his vast clinical experience.

The first chapter of this volume is devoted to the author's concept of personality. From the fundamental orientations of Jackson and Freud he conceives of the personality as being a functional unit. This concept includes the Freudian hypothesis of intrapsychic actions and their integration, together with the Jacksonian hypothesis of the evolution and devolution of mental life. The author proposes that the Gestalt method of experimental investigation be used to test these hypotheses, and he feels that the Lewinian formulations and data are particularly apt for this purpose.

Dr. Beck contends that the Rorschach test summary should represent a cross-section of the individual. This should include Lewin's concept of the present outcome of the stresses between the "higher" and "lower" activities, as postulated by Jackson, or the ego and id as postulated by Freud. The remainder of the first chapter is then devoted to a discussion of the way in which the Rorschach test functions as a projection of the ego. In the second chapter there is an extensive discussion of the types of defenses used by different persons and how they are manifested in the Rorschach examination. The author then explains the meaning of projection and discusses the interpretive meaning of the various determinants, as well as diagnostic hints to aid in understanding the individual. The hypotheses laid down in the first part of the book are illustrated in the rest of the book by a detailed study of four cases. Information from the social work and the psychiatric records is included with the Rorschach test data. While many of Dr. Beck's hypotheses are not proved, they are based on common sense and sound clinical logic. On the whole, this volume is the best of the three excellent books published thus far.

**The "Neurility" of the Kidney: A Monograph on Nerve Supply to the Kidney.** By C. G. de Muylder, M.D. Cloth. $5. Pp. 80, with 46 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1952.

The author presents the results of new studies of the innervation of the kidney with the help of improved histological techniques, and considers his results in the light of present understanding of the three fundamental processes of urine formation: filtration, reabsorption, and secretion. In addition to his own work, he presents a painstaking review of other contributions, especially a tabulation (pages 6 to 11) of previous reports on the distribution of nerve cells and fibers in the kidney. Among other interesting features is the description (page 27) of intravenous nerve endings. The book closes with a discussion of theories of hypertension, certainly a most important subject today. For the many physiologists and clinicians now doing research in this field, the concluding pages of the book will be required reading.

**S. F. A. Catalogue of Medical Films.** Revised edition of Catalogue of Medical Films published in 1948 for Royal Society of Medicine and Scientific Film Association. Cloth. 15/-. Pp. 195. Harvey & Blythe, Ltd., 212 Shaftesbury Ave., London W.C.2, 1952.

This catalogue lists over 1,000 films of medical interest that are available in England. It is arranged as follows: classified lists of films; key to distributors and owners; and alphabetical index of film titles. There are 57 subject groups and a short content description for each film.

**Fractures & Orthopaedic Surgery for Nurses and Physiotherapists.** By Arthur Naylor, Ch.M., M.B., M.Sc., Consultant in Orthopaedic Surgery, Bradford Royal Infirmary, Bradford, England. Foreword by Sir Ernest Finch, M.D., M.S., F.R.C.S., Vice-President, Royal College of Surgeons of England. Third edition. Cloth. $5. Pp. 315, with 254 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Place, Edinburgh 1, 1952.

This rather short and concise book covers all of the major diseases and deformities in orthopedic surgery. It is a very readable book. According to the title, this book is primarily for nurses and physical therapists, but it goes beyond that. There is relatively little throughout the book that concerns the nursing care of the orthopedic patient. Nurses should be taught more of nursing care than of diagnosis, differential diagnosis, and treatment, because, after all, this phase of medicine is more the responsibility of the physician than of the nurse. As for the physical therapist, the postoperative or post-treatment care in particular reference to physical therapy or physical medicine could have been stressed more.

The book is well illustrated, and almost every orthopedic disability is mentioned and described at least in brief. The book is certainly up-to-date in that the latest innovations in treatment are at least mentioned. Some of the treatment described is that of the accepted British medical opinion and is at slight variance with current American teachings. This is particularly true in the discussion of tuberculosis of bones and joints. The compactness of the book makes it a very good one, but it would seem to be a better book for junior or senior medical students, to give them an over-all picture of orthopedics, than one intended for the use of nurses and physical therapists.

**Clinical Progress in Cardiovascular Disease.** Edited by Herrman L. Blumgart, M.D., Physician-in-Chief, Beth Israel Hospital, Boston. Modern medical monographs 2. Cloth. $4.50. Pp. 143, with 6 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1952.

The second of a new series of reviews, this volume is presented as a collection of essays by 15 authorities, drawn from the "Clinical Progress" section of the monthly periodic publication *Circulation*. The essays chosen for the book were selected because of their current interest and practical usefulness.

The first section deals with a symposium on atherosclerosis, introduced by a guest editor, who poses three questions to be answered by three of the participant contributors. Their replies and the three essays that follow concerning various aspects of this controversial topic provide expert views on the significance of dietary fat and blood lipids in relation to experimental and clinical atherosclerosis. There is general agreement that further investigation is necessary to provide definite conclusions on this subject, and acknowledgment is made of the cooperation of other investigators in the field. In addition to the symposium on atherosclerosis, the book includes essays on the management of cardiac emergencies, a review of progress in surgery for mitral stenosis, management of cardiac patients in relation to surgery, and emotion and the circulation. Each essay is followed by a list of the references cited, and there is a general index provided at the end. The typography is clear, and the format is pleasing. All practitioners of medicine and clinical investigators with special interest in cardiovascular disease will find this book a convenient source of information on those phases of the subject that are of chief interest.

**Gastrointestinal X-Ray Diagnosis.** By Max Ritvo, M.D., Assistant Professor of Radiology, Harvard Medical School, Boston, and I. A. Shauffer, M.D., Instructor in Radiology, Harvard Medical School. Cloth. $20. Pp. 838, with 470 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1952.

This is an excellent reference book for the use of anyone interested in the diagnosis of diseases of the gastrointestinal tract; the clinical signs and symptoms are covered and are correlated with roentgenographic evidence to form a complete diagnostic picture of the lesions. The material is arranged in a logical sequence, and the expression is concise and readable. The illustrations are well chosen to demonstrate the x-ray findings and are reproduced in the original negatives, making them conform to everyday practice. An outstanding feature is the excellent presentation of the method of examination of the several parts of the gastrointestinal system and the anatomic and physiological basis for these methods. A comprehensive bibliography is found at the end of each subject of discussion.

# QUERIES AND MINOR NOTES

## SELF-EXAMINATION OF THE BREASTS

TO THE EDITOR:—*Please discuss the normal internal structure of mature female breasts as revealed by palpation. What palpable changes may occur as part of the monthly cycle? Is it normal at any time in a woman who has never been pregnant to feel some details of the glandular structure in one or both breasts? Does fairly frequent completely experienced coitus produce noticeable changes in the breasts? Would oral administration of progesterone for a year or more during the 10 days prior to each menstrual period cause palpable changes in the glandular structure of the breasts? Is periodic self-palpation of the breasts likely to reveal normal internal structural details, causing unnecessary fear?* *Joseph H. Toomey, M.D., New York.*

This inquiry was referred to two consultants, whose respective replies follow.—ED.

ANSWER.—It is difficult to describe the palpable picture of the normal breast. This information can be gained only by experience. There are normal variations in the breast resulting from parity, age, excessive accumulation of adipose tissue, and other factors. It is rarely possible to outline the details of the glandular structure of the breast in the nulligravid woman. Coitus does not alter the breasts, and it would not be possible to distinguish the breasts of a woman who has led an active sex life from those of one who has had no sexual experiences. Orally administered progesterone in moderate amounts does not affect the breasts. Periodic self-palpation of the breasts may result in deceptive findings, but resulting fears can be dispelled when the patient consults her physician. Self-examination does make the patient cancer conscious, but reassurance by her physician will usually suffice to remove the cancer fear. It is extremely important that women learn to palpate their breasts intelligently for most abnormal findings are discovered first by the patient, most often accidentally. Obviously, proper attention directed to the breasts must result in the much earlier discovery of neoplasms with improved results in therapy. It must never be forgotten that the breast is the commonest site for cancer in women, and it is an external lesion that should be discovered early. Thus far the patient is the physician's best ally in the early diagnosis of breast cancer.

ANSWER.—The findings on palpation of a normal breast will depend largely on the amount of adipose tissue overlying the mammary gland itself. In the thin woman, the normal breast commonly presents a definitely cordy but uniform feel, but this is likely to be imperceptible beneath the thick adipose covering of a large, fat breast. Many women experience soreness, tenderness, and, at times, sharp breast pains at and/or during menstruation (mastodynia). In some cases there is no palpable abnormality, but in others there is a palpable thickening of the breast ducts, in still others localized areas of tense, firm consistency, in some a diffuse turgidity of the entire breast, often with a "shotty" feel of the whole or a part of the breasts, with at times small cystic nodules in various parts of the breast, notably near its periphery. These all represent degrees of the benign mammary dysplasias commonly accepted as representing the response of the individual woman's breast to the ovarian hormones, especially estrogen. There is little knowledge of the role played by progesterone in such changes. More striking clinical effects of such hormone reactions are the benign cysts that may be produced, these being single or multiple, usually very small but at times as large as an egg. Even benign adenofibromas are believed by some to have a similar etiology.

Hormone therapy of such conditions should be avoided if possible, not only because it tends to center the woman's mind on her breasts, but because its results are not impressive. While some, like the inquirer, report benefit from the use of progesterone, a more rational and possibly more helpful agent would be testosterone because of its more or less antiestrogenic effect. It may be repeated, however, that hormone therapy is, in general, undesirable, especially if given hypodermically. By far the most important part of therapy is reassurance, especially when combined with simple explanations that will dispel the cancerophobia that is in the back of the minds of most such women. It is a common observation that once a woman is convinced she has no sign of cancer, her breast pains are likely to diminish or disappear. The value of self-examination of the breast is generally accepted by such organizations as the American Cancer Society, which has produced a movie as well as leaflets instructing women in the proper way to examine their breasts. Simple self-examination of this kind will certainly enable a woman to find much earlier than she might otherwise have the small hard lump that might mean serious trouble and that should impel her to seek prompt medical consultation. It need hardly be emphasized that self-examination does not mean self-diagnosis.

## AMEBIASIS IN A LARGE INSTITUTION

TO THE EDITOR:—*In a large institution, a number of patients suddenly became ill with amebiasis and died within a few days from complications, such as intestinal perforation, peritonitis, or general toxicity. Most of the patients who died resided in the same building, which houses 250 patients. The laboratory is understaffed and can only work on cases in which there are acute symptoms. A consultant suggested giving a course of terramycin to the whole population of the focus building. 1. How does terramycin therapy compare with other forms of preventive therapy, such as those described by Berberian and co-workers in* THE JOURNAL, March 1, 1952 *(page 700)? 2. How can limited laboratory facilities be employed most economically to assist in early diagnosis? 3. Is the complement-fixation test for amebiasis a reliable procedure?* *M.D., Rhode Island.*

ANSWER.—1. Terramycin has been proved effective for the symptomatic treatment of acute amebic and bacterial dysenteries. Although both terramycin and aureomycin rapidly alleviate acute dysentery, relapses frequently occur. Evidence of the effectiveness of terramyin in hepatic amebiasis is lacking. The use of terramycin in a prophylactic regimen over an extended period, as combined bismuth glycolylarsanilate and chloroquine phosphate was used by Berberian and co-workers, has not been reported. The desirability of using any resistance-inducing antibiotic for prolonged prophylactic medication is open to question until subjected to controlled study. Mass treatment (in a single course) of all inmates of a focus building with diiodohydroxyquinoline did not reduce the number of deaths resulting from hepatic amebiasis, and the incidence of positive stools was reduced only temporarily (Korns, R. F.: Personal communication). Co-medication with chloroquine diphosphate and an effective intestinal amebacide, followed by a regimen of suppressive medication for an indefinite period, appears to be the most effective means for bringing a focus building under control. Hoekenga (*J. Lab. & Clin. Med.* **39**:267, 1952) confirmed the prophylactic effect of the bismuth glycolylarsanilate and chloroquine phosphate combination against amebiasis and malaria under field conditions. Following a course of treatment, alternatively useful prophylactic medication regimens with this combination are as follows: (1) 2 tablets three times a day, one day a week; (2) 2 tablets once daily; (3) 2 tablets twice daily on two successive days of each week. For children, one-half the adult dose may be used.

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

2. Early diagnosis of amebiasis when laboratory facilities are limited is most readily and accurately accomplished microscopically by use of the zinc sulfate flotation procedure for concentrating cysts. Examination of concentrates of a series of casual stools for typical cysts is favored, because certain definite morphological criteria may be used for identification, whereas examination for trophozoites requires fresh warm specimens, use of a warm stage, dependence on characteristic motility, and extensive experience as well as critical judgment for reliable diagnosis.

3. The complement-fixation test for amebiasis is a valuable aid in the differential diagnosis of suspected hepatic abscess; it is of least value in the diagnosis of intestinal amebiasis, and a negative report does not exclude the existence of hepatic or other extraintestinal lesions.

The problem of amebiasis in mental institutions is such that the most strenuous efforts directed toward sanitation are ineffective in restricting the dissemination of Endamoeba histolytica. Under such circumstances, control of amebiasis is contingent on reducing the reservoir of cyst passers to a minimum level and instituting measures to maintain the maximum degree of suppression. The incidence of amebiasis in such institutions can be minimized by routine suppressive chemotherapy, using concurrent administration of bismuth glycolylarsanilate and chloroquine phosphate. The factors responsible for the concentration of clinically apparent cases in institutional amebiasis are not known, but the problem of amebiasis, even in the focus building, is broader than that of the acute clinically apparent cases. Acute amebic colitis is often attended by extraintestinal complications, but equally dangerous hepatic involvement also occurs in patients without a history of acute colitis, and there is no procedure available for predicting whether extraintestinal sequelae will develop in asymptomatic cyst passers. For this reason, amebiasis in the focus building must be attacked as an epidemiological problem. The incidence in such a building is usually so high that presumably all inmates would be found to be infected if examined a sufficient number of times, therefore all subjects should be treated simultaneously, and treatment must be supplemented by weekly prophylaxis. To eradicate all E. histolytica infections present and to prevent the reestablishment of the infection through transfers of patients, a one day a week prophylactic regimen should be adopted for the inmates of other buildings. If the results obtained and cost of the drug are balanced against the potential pitfalls and costs of constant policing by means of routine laboratory examinations at frequent intervals, mass chemoprophylaxis offers the most practical and economical solution to the problem of institutional amebiasis.

## INTRAOCULAR SURGERY

TO THE EDITOR:—*We have a 100 bed general hospital with two operating rooms, a minor and a major room. At present, patients requiring eye surgery are operated on in the morning in the minor room. Because of heavy schedules, the board has directed that eye operations be done in the afternoon. The question arises as to the advisability of doing intraocular surgery after the room has been used for general surgical cases, some clean and some dirty. Would there be an increased possibility of postoperative infection in eye surgery?*

*S. Henry Thaler, M.D., Huntington, N. Y.*

ANSWER.—The risk of infection at eye operations in an operating room used for general surgery is not greater because of the type of surgery done, if the usual precautions are observed. After the room is used for general surgery in the forenoon, the operating room should be cleaned, and the floor, walls, and fixtures should be thoroughly washed, rinsed with an antiseptic solution, and allowed to dry before being set up for eye surgery. An hour or more should be allowed for this purpose. Instruments and draperies may be sterilized in the same sterilizer used for general surgery, including "dirty" and traumatic cases, without jeopardizing the "clean" patient. In a large number of private hospitals, experience in operating rooms used alternately for general surgery and minor surgery shows no greater hazard for eye surgery than the use of a room for minor surgery alone. In arranging a schedule for operations in the modern operating suite, the risk of infection because of the character of general surgical cases done in the same room in any sequence is so small it can be considered not important. The nurse who supervises the operating room should have the responsibility for preparation of the rooms and should be in complete authority to determine when the rooms are safe. Cases of unusual infections and highly contagious disease, recognized breaks in sterilizing technique, faulty equipment, and a series of unexplained infections may be reasons for alterations in the scheduling of cases; however, the anticipation of such conditions need not interfere with the over-all plan when necessity and economy are better served by using the room for all types of cases.

## PERNICIOUS VOMITING AND PUERPERAL PSYCHOSIS

TO THE EDITOR:—*Has progesterone or some other sex hormone been used successfully in pernicious vomiting of pregnancy? Has this same substance ever been used in puerperal psychosis with success? I have a patient whose psychosis began three months post partum with the failure of her breasts to produce milk. What the connection is between these two events I do not know.* *Harold Inman Gosline, M.D., Provo, Utah.*

ANSWER.—Progesterone, all the sex hormones, and most other drugs have been used for pernicious vomiting of pregnancy, all with the same unpredictable results; that is, a drug that seems to help one patient only makes the next one worse. It would appear that the usual nausea and vomiting of early pregnancy are due to the increasing amounts of estrogen produced, an effect similar to that in patients given large doses of estrogen for other causes. Both types of patients become accustomed to the increase and have no further trouble. The pernicious type almost invariably has a psychic component, and psychotherapy is needed. Instilling confidence, relieving fear, and adjusting marital or personal problems usually improves these patients.

Estrogens have been used in puerperal psychoses, but it is doubtful that such therapy was of any value. Psychotherapy must be used in such cases. Whether the psychosis is puerperal, postmenopausal, or some other kind is purely coincidental. It has a basic psychic background plus a trigger mechanism that may set it off, and therapy is aimed at correcting the basic trouble. In the menopausal type, estrogen therapy may appear to be curative, at times, but actually it only relieves the disagreeable symptoms of menopause, i. e., hot flashes, nervousness, and excessive perspiration. It does not correct the underlying trouble, but it does make the patient feel better and, therefore, may be of some advantage.

## "GLOVE AND STOCKING" ANESTHESIA

TO THE EDITOR:—*What is the explanation for the "glove and stocking" anesthesia of polyneuritis? This does not follow an anatomical distribution. How can it be differentiated from an hysterical glove and stocking anesthesia?*

*Edward Dengrove, M.D., Asbury Park, N. J.*

ANSWER.—It is generally believed that the glove and stocking anesthesia pattern seen with polyneuritis is almost a mechanical problem. The nerves extending to the more distal parts of the extremities run longer courses and are, therefore, involved over a wider area and thus to a greater degree by the toxic or infectious processes responsible for the polyneuritis. The differentiation between a glove and stocking anesthesia of organic origin and one of hysterical origin is dependent on a thoroughgoing neurological examination and evaluation of the patient. The changes in reflexes and the motor involvement that may accompany a polyneuritis may serve readily to differentiate between the two. Often the sensory pattern in hysterical involvement could not have an organic basis, as for example, when vibratory sense is lost over the lower part of the tibia and intact a short distance above on the same bone, or when it is lost on one side of the sternum and present on the other, as occurs in hysterical hemianesthesia.

## CYSTIC MASTITIS

To the Editor:—*A patient with cystic mastitis has had three or four local masses removed. Do you know of any medical treatment for this condition? The patient is about 43 years old.*

*C. R. F. Baker, M.D., Sumter, S. C.*

Answer.—The only "medical" treatment for such a condition that has any basis is hormone therapy, and few would consider the results of this impressive, despite the fact that benign cystic mastitis of the type described is considered due to the effects of the ovarian hormones, especially estrogen, on the breast tissue. For this reason, such conditions ordinarily regress at or shortly after the menopause. The masses referred to are presumably multiple benign cysts, which often regress spontaneously and sometimes abruptly but often persist and become large. In such cases, they may be treated by aspiration or excision, especially when they cause constant concern to the patient despite the physician's reassurance. The responsibility of the doctor in the elimination of malignant disease in the diagnosis is, however, a serious one, and he will often wish to avail himself of surgical consultation. Many small masses in such cases, especially when they are single, call for excision and biopsy. There is still some difference of opinion among surgeons and pathologists about the exact relation of so-called cystic mastitis to malignant disease, but the majority believe that the hyperplastic types of mammary dysplasia, especially those of the so-called Schimmelbusch or Reclus type, have a definitely malignant tendency. There are many surgeons who advocate simple mastectomy in cases of this type. If and only if the inquirer feels sure that there is no malignant lesion would he be justified in a trial of hormone therapy, either with progesterone or testosterone, preferably the latter.

## HEREDITY AND ALLERGY

To the Editor:—*If both parents are allergic, will the children have a severer allergy than either parent? Will the children have the same shock organ? If both parents have allergic rhinitis, are the children likely to have asthma?*

*Robert Stock, M.D., Flushing, N. Y.*

Answer.—The incidence, intensity, complexity, and age of onset of clinical allergy depend in a large part on the dominance of allergy in the hereditary background. Children who have two allergic parents are more likely to have allergy, the manifestations are apt to be severer and more varied, and the onset will probably occur earlier in life than is the case with children who have only one allergic parent. It would naturally follow that children with bilateral inheritance have a chance of having severer allergy than that of their parents. It should be remembered, however, that, whether one or both parents are allergic, it does not necessarily follow that the child or children will have clinical manifestations of allergy. The shock organ tendency is not inherited to the same degree as is the general predisposition to allergy. Nevertheless, there is a tendency in many families to have a particular predominating clinical manifestation. Children are more likely to have asthma if their parents had it than if their parents had had only hay fever, urticaria, or eczema. Thus, the children referred to in the query are not as likely to have asthma as they would be if their parents had asthma. Again, it must be borne in mind that this is only a pattern. Asthma may develop in the children of parents with allergic rhinitis.

## CLINICAL USE OF NYLON

To the Editor:—*Is there any data concerning the hypersensitivity of human tissues to nylon? I am especially interested in tolerance to nylon orthopedic prostheses.*

*Robert H. Hutchinson, M.D., New Orleans.*

Answer.—Nylon is well-tolerated by tissues. In rare instances, dermatologists have found patients to be sensitive to nylon. Following are excerpts from articles by authors who have used nylon clinically:

"Black silk, terylene, nylon and human hair all produce a histiocytic and giant-cell response, and from the present observations it is not possible to discriminate between them. In our opinion, silk of a calibre of 5/0 is still the best available material for nerve suture." (Mukherjee, S. R., and Douglass, D. M.: *Brit. J. Surg.* **39**:271-277 [Nov.] 1951.)

"Range of painless motion can usually be obtained by arthroplasty with nylon membrane. To date we have observed no reaction to the nylon membrane." (Kuhns, J. G., and Potter, T. A.: *Ann. Rheumat. Dis.* **10**:22-30 [March] 1951.)

"Nylon fabric may be used in various operative situations where either fixation or motion are desired. The quality of nylon fabric with particular reference to its weight and mesh is related to tissue reaction to it. Nylon is well tolerated, apparently indefinitely. Success of operation is not reckoned to be due to the use of nylon fabric alone. It overcomes only the technical factors of fixation or gliding as the need may be." (Burman, M.: *Bull. Hosp. Joint Dis.* **9**:205-208 [Oct.] 1948.)

"Knees with fibrous adhesions and severe interarticular derangement function better with nylon interposition than with simply synovectomy and debridement alone. No extensive reshaping of the articular surfaces is desirable. It is never necessary to lengthen the quadriceps tendon in order to secure flexion." (Kuhns, J. G., and Potter, T. A.: *Surg., Gynec. & Obst.* **91**:351-362 [Sept.] 1950.)

## ABDOMINAL PAIN AFTER AN APPENDECTOMY

To the Editor:—*In Queries and Minor Notes May 3, 1952, page 98, a man was said to have recurrent abdominal pain that came on a month after an appendectomy and was not relieved by reexploration of the abdomen, which showed only a few adhesions. The possibility of a regional ileitis was considered as the likely cause. Comments on this communication by Dr. Leon J. Taubenhaus are of interest, since his remarks represent an every day experience in the practice of many physicians (J. A. M. A.* **150**:66 *[Sept. 6] 1952). Too often the physician gravitates toward neurosis as his diagnosis when he is unable to explain a pain that should have been cured by his treatment. It is easy to explain our mistakes in this simple manner, since it satisfies the physician, but unfortunately it fails to offer the patient the relief he seeks.*

*I have encountered a small series of patients who have had not only an appendectomy but, subsequently, several exploratory operations for adhesions, without relief of lower right quadrant pain. Indeed, some of these patients have also had kidney examinations, including cystoscopic examination, lower right bowel studies, and even a herniorrhaphy, without relief of pain in the lower right quadrant. Characteristic of this pain is the fact that it is aggravated in recumbency and relieved by activity.*

*I believe that the picture described above is that of referred segmental pain originating somewhere between the ninth thoracic and first lumbar spinal segments. The most probable cause of such pain is a postural defect, commonly a mild scoliosis. In the majority of the cases of lower right quadrant pain in which a scoliosis is found that have come to my attention, the left lower extremity is found to be longer than the right, resulting in a convexity of the lumbar curve to the right. Often, the pain is relieved by equalization of limb length simply by adding a lift to the short leg. Oftener, exercises for the back, a rigid bed, and hot baths will relieve most of the symptoms. These symptoms can also be caused by a higher than usual herniated intervertebral disk or even by a cord tumor; however, these are rare compared to the frequently found postural defect. The vague and bizarre pictures that can arise from referred pain of a segmental character either of dermatome or sclerotome patterns have been well described by Kellgren and Lewis of England. They have been able to produce visceral-like pain in the lower right abdomen by simply injecting 0.1 to 0.3 cc. of a 6% sodium chloride solution into paravertebral muscle opposite the 11th thoracic and 12th thoracic spinal segments on the right side. Much more work needs to be done in this interesting field. I feel certain that many diagnoses of neurosis will be eliminated if the physician will consider the possibility of referred pain to the abdomen caused by minor skeletal defects of the spine.*

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